JOURNAL

OF THE

INDIAN MEDICAL ASSOCIATION

Vol. X *Calcutta, July, 1941* No. 10

CHRONIC MASTOIDITIS

B. TIRUMAL RAO, F.R.C.S. (Edin.), D.L.O. (Lond.)
Surgeon, E.N.T. Department, King George Hospital, Vizagapatam.

The development and the course of suppurative inflammation of the middle ear cleft may be classified for purposes of clinical description into three divisions:

1. Acute suppurative otitis media and acute mastoiditis. 2. Chronic suppurative otitis media and chronic mastoiditis. 3. Intracranial complications arising from 1 and 2.

While the disease is acute, the patient is prompt in seeking relief; the diagnosis comparatively easier; the lines of treatment are more clearly defined and the prognosis is considerably more favourable. It may necessitate a myringotomy or a simple mastoidectomy (Schwartz's). Complete resolution takes place in at least 80 per cent of the cases. In a very small percentage of cases where the inflammation takes a fulminating course, intracranial complications arise which are very serious and the prognosis then is very grave indeed.

But the rest of the cases pass into a stage of chronic otorrhœa with all its attendant dangers and disabilities. The patient does not generally take it seriously, till an intracranial crisis is actually precipitated. The prognosis is less favourable and lines of treatment are less well defined and a successful termination is less likely. It is hard to differentiate between chronic conditions in the middle ear and those in the mastoid process. There is probably present some bone disease either of the ossicles or the walls of the antrum or the tympanum, in a great number of cases of chronic suppurative otitis media. The usage of the term chronic mastoiditis indicates that chronic suppuration of the middle ear has progressed to a stage when it demands surgical treatment. It is more of a clinical rather than of any pathological significance.

Etiology

The causes of chronic mastoiditis are, of course, the causes of chronic suppuration of the middle ear and the latter again is only an end result of unresolved acute suppuration. Of the factors which tend to chronicity, the foremost is the lack or inefficiency of treatment in the acute stage. As Sydenham put it "Acute disease is an act of God; of chronic disease the patient himself is the author." That is why it is far more common in the poorer classes of people.

If the infection is of low virulence and the drainage adequate, suppuration readily ceases and the tissues are restored to their normal condition. Chronic suppuration is especially frequent in cases due to measles, diphtheria, influenza and other infectious

fevers. The presence of a nasopharyngeal infection is an additional factor in keeping up an aural discharge.

Another factor which has been credited with playing an important role in the course of middle ear suppuration is the structure of the bone itself. According to Cheatle, the mastoid part of the temporal bone contains in infancy no cells with the exception of the tympanic antrum, which is of considerable size and a layer of small cells in its outer wall. The further development of cells varies in type, sometimes developing into a pneumatic and cellular type, sometimes into an entirely diploetic and acellular type or again into a mixture of both forms. The distribution of the cells themselves varies in different bones and the sight of abscess formation in acute mastoiditis depends upon the predominance of cells, giving rise to the well known zygomatic or Bezold's or petrous type of the disease. According to older teaching, the dense bone which surrounds the antrum in cases of chronic middle ear suppuration was put down to sclerosis due to a long standing suppuration. Cheatle's researches, however, point out that this is not the effect but the cause of chronic suppuration. In cellular type of mastoid its inner and outer tables as well as the intervening partitions between cell and cell are so thin that in an acute inflammation extending to the bony structure, it goes into a rapid process of necrosis and abcess formation. In the acellular type of bone, if the infection is virulent, it becomes chronic with the formation of granulation tissue and cholesteotoma. The dense bony wall prevents the rapid spread of inflammation to the surface and become manifest as an acute abscess outside.

It must be mentioned also that Wittmark insists that the dense type of mastoid is really a pathological one and is due to infantile otitis media which has interfered with the normal absorption of the diploe and the proper pneumatisation of the bone. There is also the possibility, it cannot be denied, that an originally pnuematic mastoid may become dense as a result of recovery and repair of acute mastoiditis, the granulation tissue in the air cells having been replaced by new bone formation. But this occurrence is very uncommon. The dense mastoid process appears in a large majority of cases to be developmental in origin and is found to make a distinctive contribution to the chronicity of the suppurative condition of the middle ear.

Pathology

The mucous membrane is swollen and hyperæmic. It encroaches upon the cavity of the antrum and the cells. The discharge tends to collect and to consist of more and more of desquamated cells. If there is any scope of drainage into the tympanic cavity, it is manifested in the form of chronic otorrhœa either intermittent or continuous. Where the epithelial covering is completely denuded, granulations form which erode the bone leading to caries and destruction. The bone is ulitimately perforated. If the perforation is on the outer table of the mastoid, it produces periostitis and a superficial subperiosteal abscess. If the inner table is perforated, intracranial structures are brought into direct contact with the inflammatory process with its possible dangerous developments.

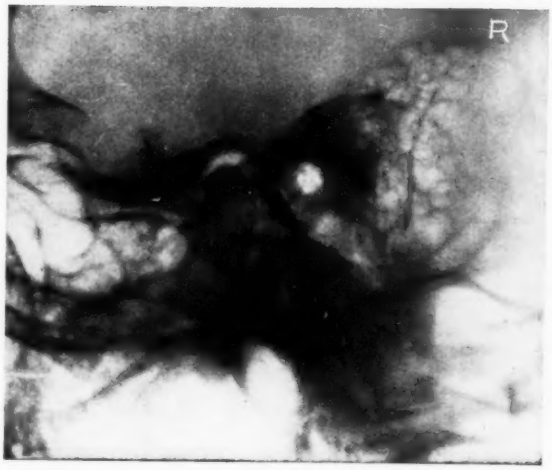
Symptoms

The victim of chronic mastoiditis may go about for long without the slightest idea of the seriousness of the disease which has overtaken him. So long as the drainage is free, there is little pain or discomfort. The existence of such a focus of infection is very likely to affect his general health. But the cause of his ill health is often overlooked. As the process extends and the drainage is impeded certain symptoms manifest themselves, whose import is no longer ignored either by the patient or his medical attendant.

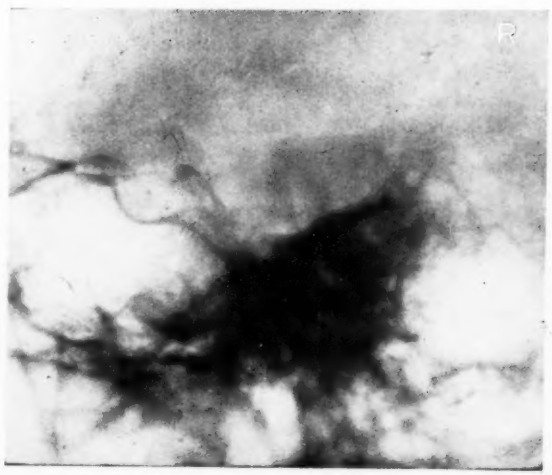
Firstly, where the inflammation has extended to the outer table of the mastoid, there is pain and tenderness and local œdema. The character of the discharge furnishes another very useful indication. Excessive discharge, its sudden and painful cessation or its intermittent character accompanied by or alternating with pain, its grossly purulent and fœtid character, its yellowish green or reddish brown colour streaked with blood are the important points to notice.

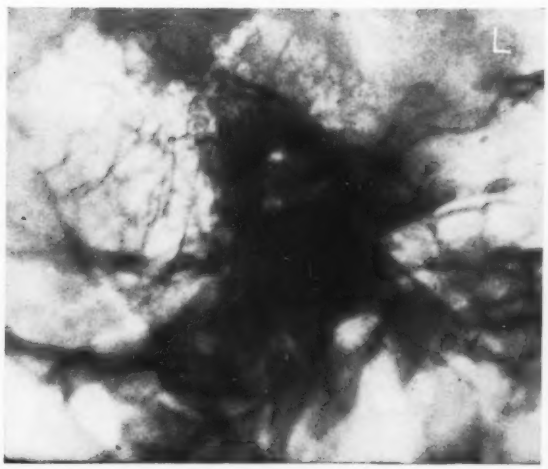
There may be very little fever in an uncomplicated case. Pain deep seated in the mastoid region or radiating to the temporal and parietal or occipital regions, vertigo, nystagmus, strabismus, rigors are indications of a breaking through of the necrotic process into the cranial cavity, or the labyrinth.

The chief objective signs which afford indication of the necessity of surgical exploration of the mastoid are:



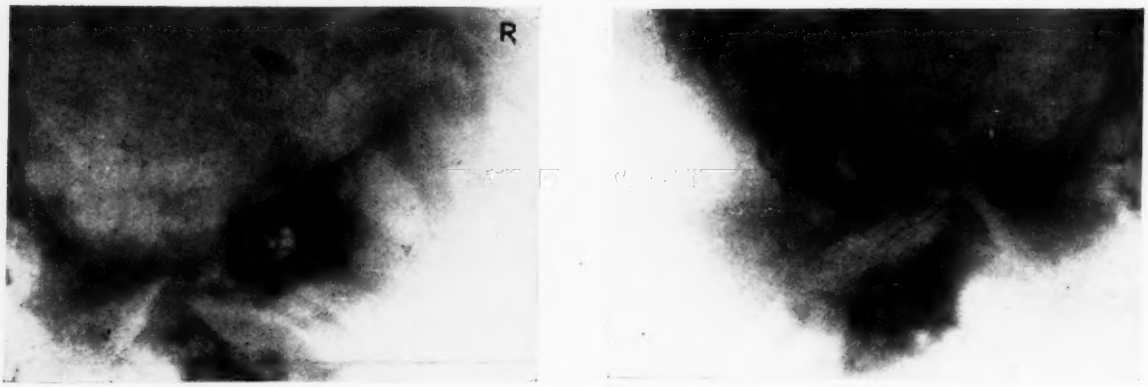
Radiograms of mastoids in a patient aged 20 years. Note the cellular appearance of the right mastoid and the acellular appearance of the left mastoid which is the diseased one. This patient was admitted with left sided facial paralysis.



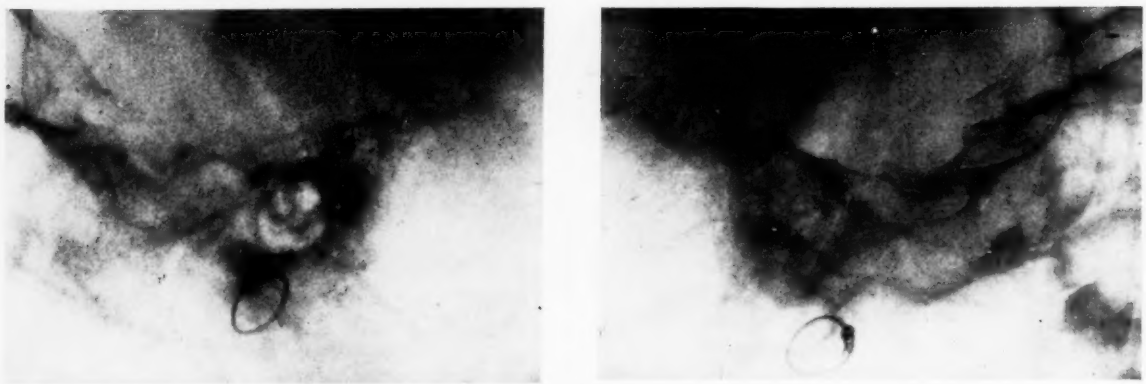


Radiograms of mastoids in a patient aged 35 years. Note the large cellular left mastoid and the abscess cavity in the right mastoid.

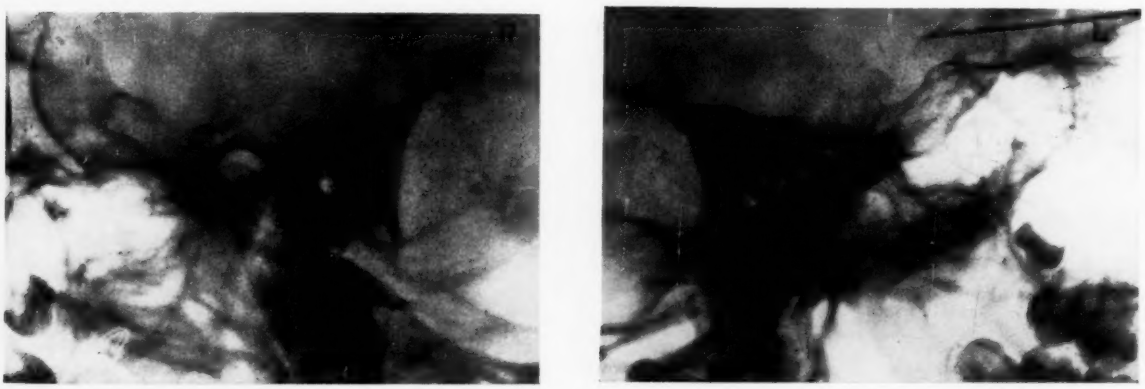
Engraved & printed by
The Bengal Autotype Co., Cal.



Radiograms of mastoids in a child aged 1 year. Note the absence of any cells and the semicircular canals.



Radiograms of mastoids in a child aged 4 years. Note the presence of cells in the right mastoid and the loss of circular appearance in the left mastoid which is the diseased one.



Radiograms of mastoids in a child aged 10 years. Note the completely acellular nature of both mastoids.

1. A discharge which remains fœtid inspite of careful and persistent treatment. 2. A posterior marginal or attic perforation indicating the presence of bone disease. 3. The presence of a polypus or granulations which recur rapidly after removal. 4. Subperiosteal mastoid tenderness, swelling, or the presence of a sinus. 5. Facial paralysis.

Treatment

The aims of surgical treatment are:

1. To make the patient safe as regards intracranial complications such as extradural abscess, lateral sinus thrombosis, meningitis, brain abscess and facial paralysis. 2. To preserve the hearing. 3. To cure otorrhœa. 4. To avoid the necessity of prolonged supervision.

The accepted method of operation has long been the radical mastoid operation. It achieves, no doubt, in a large number of cases the first and the foremost of the above objects, *viz.*, the prevention of intracranial complications, but hearing is very often impaired, the discharge does not always disappear, and in any case prolonged supervision is necessitated. To obviate these disadvantages, attempts have been made to simplify and better the procedure. It is aimed at not to do any set operation preconceived, but to adapt and modify the procedure as it suits each individual case in accordance with the pathological findings on exploration.

The Schwartz's operation which merely excentrates the mastoid antrum and cells and completely removes all diseased bone from the mastoid, is all that is necessary in early cases of chronic otorrhœa especially in children, when there are no granulations or polypi or cholesteotoma and when the discharge is more mucoid or mucopurulent in character. If after exploring the aditus, it is found that the attic shows signs of disease, the outer wall is removed. This improvement over the original Schwartz's operation has been named the conservative operation. Both procedures have been termed as simple mastoid operation in this series of cases. In both these procedures the external auditory meatus as well as the middle ear contents are left undisturbed. There is no meatal plastic operation and the cavity is partially closed except when the dura is exposed.

When the simple operation is contra-indicated, the antrum is opened and diseased bone removed. The posterior meatal wall is removed, leaving sometimes the bridge in tact. The outer attic wall is next removed. The ossicles are left alone except the incus which sometimes comes off. This is called the modified radical operation.

The radical mastoid operation is reserved for cases with gross destruction of the tympanic membrane, ossicles and those with intracranial complications, and with gross destruction of the walls of the tympanic cavity. In this operation the contents of the middle ear, the incus, the malleus and the tympanic membrane are all removed along with the mucous membrane.

In the modified radical and the radical operations the meatal plastic is performed either at the same sitting if dura is not exposed and if there is no likelihood of any intracranial complications, or later when necessary, at a second sitting when the wound begins to properly heal.

Review of Cases

Having discussed briefly the subject in general and the methods of surgical procedures adopted in its treatment, I shall now proceed to present a short review of cases treated here during the decade 1929-38.

The total number of patients treated were 108 as against 246 cases of acute primary mastoiditis treated during the same decade. 71 were males and 36 females. The total number of operations performed were 110, two of the patients having had double mastoiditis. The marked disparity in sexes treated is noticed in the case of acute mastoiditis also. This is in strong contrast with the English and American statistics, where both the sexes are represented in almost equal numbers.

1 to 10 years of age	41
11 to 20 „ „	27
21 to 30 „ „	18
31 to 40 „ „	10
41 to 50 „ „	9
51 to 60 „ „	2
61 to 70 „ „	1

It will be observed that about 80 per cent of the cases were under 30 years of age.

Etiology—In a few cases colds, influenza have been given as the cause but generally it has not been possible

to get any history that is reliable. Trauma was the cause in three cases. In one patient the trouble started with the instillation by mistake of pure carbolic acid into the ear. Fortunately the patient was cured by doing a simple mastoid operation, with perfect recovery of his hearing.

Otoscopic Appearances—

Polypi were noticed in	.. ..	17 cases
Granulations were noticed in	..	22 ,,
Discharges were noticed in	.. ..	103 ,,
Marginal & attic perforations were noticed in		34 ,,

Findings at Operation—Subperiosteal abscesses were found in 12 cases. In 16 cases a sinus in the cortex of the bone was come across. Cholesteotoma was found in 17 cases. A large sequestrum was removed in 5 cases. In only one case the mastoid was found to be cellular. The operative finding of this acellular character of the mastoid, is in general conformity with the x-ray findings that was obtained whenever possible.

Radical operation was performed on 41 cases, modified radical in 42 cases and the simple in 27 cases. As one could observe from the above figures the majority of these operations were performed upon cases which were in the stage of an acute exacerbation of a chronic mastoiditis. Therefore, the indications for surgical interference were absolute and the operation often nothing less than a lifesaving measure.

Results—Of the 108 patients treated by operation, 100 were discharged cured and 8 of them died. Two were admitted with symptoms of meningitis. Four of them developed meningitis after the operation. Of the latter group, one was a boy who had maggots in the ear previously, another was a diabetic, the third was an aged man of 70 years and the fourth one was of tuberculous infection. There was only one case of lateral sinus thrombosis. The lateral sinus was exposed and drained and the internal jugular vein was ligated but the patient did not make a recovery. Lastly, there was a small girl of 10 years of age who ran a septicæmic temperature and died. There was no case of brain abscess in this series. Of the other intracranial complications, there were four cases of perisinus abscess and two of extradural (middle fossa) abscess, who have all made a complete recovery after operation.

The total number of patients who were lost out of complications developed after the operation is six. Thus it must be admitted that the primary object of surgical intervention in this disease, namely to prevent the onset of intracranial complications, has not been fulfilled as satisfactorily as it ought to be. But no operation is entirely safe in a field with such close and dangerous neighbours as the lateral sinus, the labyrinth and the dura. The general condition of the patients is no less an important factor in determining the prognosis. Moreover, this series relates to the decennium just preceding the free use of Prontosil group of drugs in the control of bacterial infections. In spite of all these considerations, it is only proper to point out here that the results can be viewed even with this much of complacency only on the assumption that all the rest of the patients who were discharged cured remained free from further trouble. On this point as well as with regard to the preservation of hearing and the cure of otorrhœa, it is regretted that no statistical data with any degree of accuracy can be given. We are still developing our system of "follow up" of cases. The average stay in the hospital was between four to six weeks. This cannot be considered as too long a period considering the nature and situation of the operation.

Conclusion and Summary

The clinical import of the term chronic mastoiditis as applied to cases of chronic suppuration of middle ear is clearly stated. Its etiology with special reference to the important role of the anatomical structure leading to chronicity, illustrating with radiograms, the pathology, symptoms, the indications and aims of surgical treatment and the different types of operative procedure adopted for the purpose are briefly discussed. A review of 10 cases treated during the decade 1929 to 1938 is presented. The importance of the follow up of cases for a proper assessment of the success of treatment is laid stress upon.*

*Read at the Scientific Section of the XVII All India Medical Conference, Vizagapatam, Dec., 1940.

CHEMOTHERAPY OF BACTERIAL DISEASE WITH REFERENCE TO SULPHONAMIDE GROUP OF DRUGS*

B. N. GHOSH, M.B.E., F.R.F.P.S. (Glas.), F.R.S. (Edin.), F.S.M.F.

Professor of Pharmacology Carmichael Medical College, Calcutta

Search for remedies for the treatment of disease can be traced from the earliest history of man. And drugs in different forms were used without any knowledge of their physiological action, or the etiology, pathology or symptomatology of the diseases treated. Nevertheless some of these remedies which were used empirically are to-day occupying important positions and are valuable means of treatment in our hands. The use of cinchona in malaria and of mercury in syphilis are instances in point. These drugs were used centuries before we had any knowledge regarding the causation of the diseases against which they were employed. We now use these drugs not empirically but can furnish sufficient explanation regarding their action. But as long as the value of medicine remains in part unexplored, there will remain grave conditions which must be met by empiricism; and as long human beings in health and sickness vary individually as to their symptoms and relative powers to disease and drugs, there will be fields which must be dealt without the accuracy given us by the laboratory worker. The most logical and the most successful treatment is one which will eliminate the cause of the disease. Unfortunately, however, in many cases the origin of the disease may baffle the most careful and skilful observer, in other instances the cause, though discoverable, may be beyond the power of chemical and mechanical agents at our command to affect Thus we may know that dyspnœa and œdema are due to lesions of the valves of the heart, but we know of no means to repair the damaged valve; yet we can rationally attempt to antagonise the results of the pathological lesions. Thus in endocarditis we have for our object to increase the functional power of the heart muscle, so that notwithstanding the disadvantages under which it labours, the heart may still be able to fulfil the necessities of circulation.

The use of quinine in malaria and of mercury in syphilis are examples of chemotherapy. This term has been restricted by Ehrlich to the parasiticidal treatment of infections by chemical agents.

In 1909 Ehrlich sought systematically to extend the field by the search for substances which will combine a relatively high toxicity for the parasite with a relatively low toxicity for the host, *i.e.* the drug should have a high chemotherapeutic index.

A deliberate search was made for a remedy for an infection from a group of nearly related chemical compounds, one of which is known to possess a specific action on the disease in question. Not only a great impetus but a new orientation was given to investigation of this kind by the genius of Ehrlich. In this way a whole series of arsenical compounds was investigated with a view to discovering one which would have a maximum parasitotropic with minimum organotropic properties.

Till lately most of the chemical compounds introduced as chemotherapeutic remedies were applied in relation to protozoal diseases, *viz.*, malaria, leishmaniasis, trypanosomiasis, amœbic dysentery, etc. Any attempt to apply this investigation to bacterial diseases was unsuccessful, for most of the antiseptics and disinfectants have no specific action on the microbes in preference to the tissues in which they were embedded, and that most of them are protoplasmic poisons. Destruction of the septic organism in a wound surface entails the destruction of the surrounding cells also. Therefore, disinfection can only be carried out in a part in which the superficial cells are not of vital importance and may be restored by new tissue growths. It is, therefore, impossible to disinfect the body as a whole, as is necessary in bacterial invasion of the body, because a drug circulating in the blood in sufficient concentration to destroy the bacteria will be equally detrimental to the organs in which they are embedded. Many investigations have been made in this quest to find a substance which when introduced into the body will differentiate between the protoplasm of the bacteria while leaving the tissues of the human host unaffected. The sterilisation of the blood stream against some bacterial infection was looked upon as an unattainable

*Burdwan Trust Lecture delivered at the Ronaldshay Medical School, Burdwan on 6th February, 1941.

ideal till the discovery of the drugs which we will discuss to-day, namely, the sulphonamides.

Historical

We can only trace briefly the development of this important group of drugs. Gelmo in 1908 first described para-amino-benzene-sulphonamid (Sulphanilamide). A year later Horolein, Dressel and Kothi prepared the first azo dyes with sulphonamid and substituted sulphonamide group and found that they were characterised by greater fastness to washing and milling. Isenberg demonstrated the bactericidal action of certain azo compounds *in vitro* and employed Chrysoidine for chemotherapeutic purposes but not the slightest therapeutic effect could be obtained in infected animals. Many investigations were made which ultimately led to the discovery of azo compounds with marked bactericidal properties *in vitro* but no action *in vivo* in the mouse. In studies confined to compounds containing the sulphonamid groups and tested only by animal experiments, drugs effective against streptococcus infection were discovered. In 1932 Mitzsch and Klerer obtained a patent for the azo dye,—Sulphanido Chrysoidin (4-sulphamido—*2'*:*4'*—diaminoazobenzene) which was found by Domagk to cure an otherwise fatal streptococcus infection in mice. This compound was placed in the market under the trade name of "Prontosil". A more soluble compound, for intramuscular injection was described shortly and was called Prontosil Soluble or Neoprontosil. Even before the appearance of Domagk's paper in 1935 mention of the treatment with "Streptozon" (prontosil) of patients with infections appeared in German clinical journals and afterwards numerous favourable results in human infections were reported, but it was only after the publication of the paper by Colebrook and Kenny on the marked beneficial effect of prontosil in puerperal sepsis that much interest was awakened in the English speaking countries on these new compounds. (Marshall, Jr.).

Chemistry

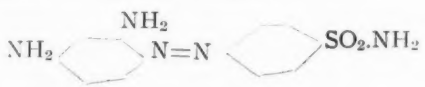
At the present moment there are numerous preparations of this group and it is therefore necessary to study their chemical structure. It will be more convenient to start with Sulphanilamide itself, the simplest of the sulphonamides, the mother substance of all the other derivatives.

Sulphanilamide is para-amino-benzene-sulphonamide. If to a benzene ring <⬡> one amino group H_2N is combined, aminobenzene or aniline is formed. If to the amino benzene NH_2<⬡> the sulphonamide group is attached and to the para position one to the other, we get para-aminobenzene sulphonamide, or aniline sulphonamide, which has been contracted by Fuller (1937) to sulphanilamide.

Thus from sulphanilamide two types of compounds are possible by substitution of (*i*) NH_2 (amino) and (*ii*) $SO_2.NH_2$ (sulphonamide group). We shall now consider the commonly used compounds that fall into these two categories.

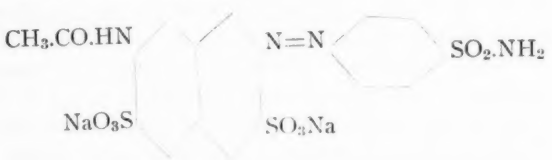
A. Compounds formed by the substitution of "Amino Group"

1. Prontosil or Prontosil Rubrum



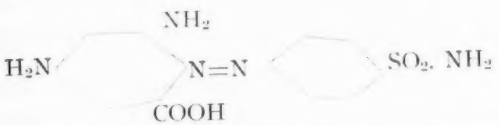
4:sulphonamido-2':4'diamino azo benzene

2. Prontosil Soluble



Disodium salt of 4'sulphonamidi-phenylazo-1-hydroxyl-7-acetyl-amino-naphthelene-3:6 disulphonic acid

3. Rubiazol



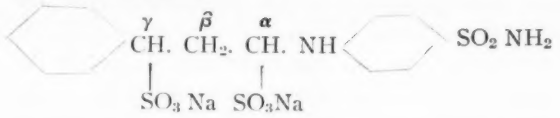
6-carboxy-4-sulphonamido.2'-4'-diamino azobenzene

N.B. Differs from prontosil in possessing COOH (carboxyl) group.

4. Proseptasine

p-Benzylaminobenzenesulphonamide

5. Soluseptasine

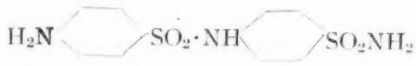


Disodium-p- (rphenylpropylamino) -benzenesulphonamide- γ-disulphonate

6. Para-acetyaminobenzenesulphonamide
(Inactive form, *i.e.*, in the form excreted)

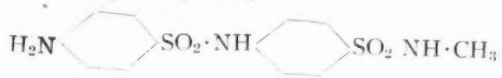
B. Compounds formed by substitution of the Sulphonamide Group

1. Diseptal C(DB32)



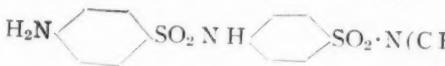
p-aminobenzene-sulphonyl-p-aminobenzene-sulphonamide

2. Diseptal B(DB87)



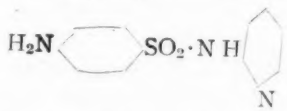
p-aminobenzene-sulphonyl-p-aminobenzene-sulphonemethylamide

3. Uleron(DB90, Diseptal Auleron)



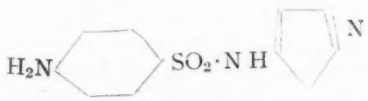
p-aminobenzene-sulphonyl-p′-aminobenzene-sulphonedimethylamine

4. Sulphapyridine, M & B 693, Dagenan



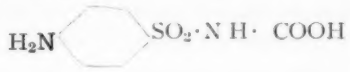
2(p-aminobenzenesulphonamide) pyridine

5. Sulphathiozole, M & B 670



2(p-aminobenzenesulphonamide)thiozole

6. Albucid



p-aminobenzene acetylsulphonamide

Note. Acetyl group when joined with sulphonamide group forms an active compound unlike when joined with amino group.

Chemical Constitution and Chemotherapeutic Activity

In order to obtain increased therapeutic activity with a wider field of application and a lowered toxicity so much modification has been instituted by introduction of various radicals and so many hundreds of compounds have been examined that a consideration about them naturally limits itself to certain broad, general and qualitative remarks.

The works of Fourneau *et al* as summarised by Findlay (1940) will serve to illustrate this point.

(a) *Influence of the relative position of the sulphonamide and amino groups* of the three isomers, the ortho and meta sulphonamides were devoid of action.

(b) *Replacement of the sulphonamide groups* ($SO_2 NH_2$) by various other groups produced inactive compounds *e.g.*, NH_2 (amino group), CN(cyanide group), $CO NH_2$ (carbamide group) etc.

(c) *Substitution in the sulphonamide group.* Alkalination does not suppress activity, but, at least in the higher members of the series, decreases it in proportion to the weight of the substituted alkali radicals.

(d) *Replacement of the amino group by another radical.* The parahydroxy derivative is highly active; the para methyl derivative is inactive.

(e) *Derivatives of constitution of the amino grouf.* When the amino groups of para aminobenzene sulphonamide is replaced by CH_3 CONH acetamide or the like, the resulting compounds are active.

(f) *Azo-compounds with substituents in the sulphur free nucleus.* A number of mono, di, and trihydroxy derivatives of the second nucleus are active.

(g) *Addition of a third constituent in the benzene nucleus.* This is followed by a decrease of activity.

The above is only an outline of the extensive work done on the subject by various workers. Of the many compounds examined some are inactive or inferior to sulphanilamide, while others are equal or superior to it. Thus the water soluble sulphonic acid compounds

of sulphanilamide, such as camphor-sulphonate, which contains only 40 to 50 p.c. sulphanilamide, are experimentally found to be equal or greater in activity than sulphanilamide itself.

It has, however, now been shown that sulphonamide group is not necessary for activity. Thus 4:4 diamino-phenyl sulphone, and 4:4 dinitro-phenyl sulphone though differing in chemical structure from sulphanilamide and without any possibility of their yielding sulphonamide grouping in the body have been found effective; and at the present moment engaging much attention; one of the important being "Rodilone" (4:4 diacetyl amino-diphenyl sulphone) with greater activity and lower toxicity than the sulphanilamide.

The two types of compounds that formed by the substitution of either of the amino group or of the sulphonamide group differ in their toxicity and range of activity. Thus in the benzyl derivative of para aminobenzene sulphonamide (Proseptasine) the toxicity is greatly reduced, whereas the introduction of pyridine nucleus in the sulphonamide group of para-amino benzene sulphonamide has resulted in a compound with a wider range of activity.

Table showing toxicity of various compounds and comparative efficiency in expierimental infections in 20-grm mice (WHITBY, *Lancet*, 1937)

Compound	*Infections*	*Dose Mg.*	*Efficiency figure with maximum possible in paranthesis*	*Toxicity to 20 Gm. mice*
Prontosil sol. subcutaneous ..	Strepto	7·5	6·8(10)	80 mg. (subcut) is tolerated.
p-aminobenzene sulphonamide ..	Strepto	25·	7·7(10)	Markedly toxic at 50 Mg. fatal at 150 Mg.
	Meningo	25·	4·1(7)	
	Pneumo Type I	25·	1·2(7)	
p-benzylaminobenzenesulphonamide	Strepto	50·	7·9(10)	Non-toxic at 200 Mg.
	Meningo	50·	0·6(7)	
	Pneumo Type I	50·	0·5(7)	
Disodium-p phenyl-propyl amino-benzene sulphonamide a-r-disulphonate	Strepto	10·	6·6(10)	Slightly toxic at 200 Mg.
	Meningo	10·	0·8(7)	
	Pneumo	30·	0·9(7)	
4:4 diamono benzene sulphanilamide tartarate	Strepto	10·	7·5(10)	Non-toxic in doses of 100—160 Mg.
	Meningo	10·	4·2(7)	
	Pneumo Type I	10·	3·0(7)	
4:3' diaminobenzene sulph. ..	Strepto	20·	7·1(10)	Non-toxic in doses.
	Meningo	20·	1·2(7)	
	Pneumo Type I	20·	4·0(7)	

To this is added the average lethal dose of M & B 693 per kg. of body weight, for mice 16·6 gm. and 15·8 gm. for rabbit.

The acute toxic symptoms produced in experimental animals are referable chiefly to the central nervous system. In mice there is in-co-ordination and paralysis, in rabbits rigid extension of the limbs with contraction of head resembling decerebrate rigidity, dyspnœa; in dogs the symptoms resemble administration of large doses of ethyl alcohol.

Chronic toxic manifestations are interesting. Hageman in mice found sublethal doses of sulphanilamide given intraperitoneally for some days producing eosinophilia in the bone marrow, deposition of hæmosiderin in the spleen and a fibroblastic foreign body reaction to crystals of the drug, on the surface of the liver, spleen, and kidney. In rats given with food caused a marked increase in urinary and fæcal porphyrin; spleen engorged with deposit of greenish brown granular pigments; loss of weight in some instances was observed.

Sulphapyridine in doses of 3 mg. for 15 days in rats produced no increase in the excretion of porphyrin in the urine.

Degenerated changes in the anterior horn cells and some of the cortical cells of cats were found after large doses.

Oakley (1937) working with prontosil noted amongst other things concretions of various sizes of the dye in the much dilated straight and convoluted tubules. In this connection the observations of Stewart *et al* (1938) on the possibility of calculus formation from sulphanilamide which has been shown to be precipitated in the urine at room temperature is worth remembering. Deposits of calculus following the use of sulphapyridine and sulphathiozole has also been reported.

Absorption, Distribution, Fate and Excretion

Both in animal and human subjects sulphanilamide when given by the mouth is quickly absorbed and the process is complete in 3-4 hours. Absorption is quicker if given in solution than in capsules or tablets. Alkalies hasten absorption. After a single dose the peak in blood concentration is reached in 3 hours; thereafter the concentration falls gradually to zero during the following 24 hours. With repeated administration at intervals of 4-6 hours a blood concentration of 20-10 mg. per 100 c.c. can be obtained and maintained. The optimum blood conc. to be effective is 10 mg. per 100 c.c.. The persistence in the blood has been ascribed to reabsorption in the renal tubules of about 75% of the drug in the glomerular filtrate. With impaired renal functions the blood concentration is raised both early and higher. Subcutaneous injections do not give a higher concentration in the blood than that is obtained by oral administration.

Prontosil 'S' is more or less equally absorbed, whereas Prontosil Rubrum is less quickly absorbed. Sulphapyridine is also *slowly* absorbed in comparison to sulphanilamide. In the case of more insuluble compounds such as Uleron as much as 60% may fail to be absorbed.

The rate of absorption varies widely in different individuals, but unfortunately it is much slower in diseased than in a normal person.

On entering the blood sulphanilamide quickly penetrates all the fluids and tissues of the body and it appears to be distributed like alcohol or salicylates or urea. The distribution is more or less uniform, though the bone and the fat contain relatively less. In addition to normal body fluids, such as saliva, sweat, tear, etc., it is also found in pathological exudates, *e.g.* in pleural effusion. In normal secretions of the cervix uteri it is probably present in insignificant amount. It passes readily into fœtal blood and amniotic fluid. It has been found in the human breast milk. In the cerebrospinal fluid its concentration is about 75% of that in the blood and the drug appears to pass as readily into the cerebrospinal fluid of the patients suffering from meningitis as that of healthy subjects.

Sulphanilamide remains both in free and conjugated forms, the latter as the inactive acetyl derivative, para-acetyl-aminobenzene sulphonamide. Acetylation probably takes place in the liver. The acetylated compound has no bactericidal action and is toxic to the host, but fortunately it is excreted rapidly.

The drug is chiefly excreted by the kidneys both in free and conjugated forms, entirely by glomerular filtration. Of the drug in the glomerular fitrate 70 to 80% is reabsorbed by the tubules; diuresis will thus favour excretion of the drug and a state of impaired renal function will have the opposite effect. After a single dose the excretion is complete after three days. After the same period with repeated doses a state of equilibrium is obtained between the amount of drug taken and the amount eliminated. To obtain an adequate concentration in the blood it is necessary to use the drug at first in large doses and then to follow this with a smaller maintenance dose.

Mode of Action

All observers are agreed that both the prontosils are devoid of any action on streptococcus *in vitro,* whereas sulphanilamide possesses great activity not only *in vitro* but also *in vivo*. This and the fact that even prontosil when administered by the mouth is excreted as sulphanilamide in the urine, indicate that p-amino-benzene sulphonamide is the bactericidal substance of prontosils active in the body. Though the majority of workers subscribe to this view, yet on the continent it is still held that prontosil *per se* may have some activity in the tissues, or that it may be converted into some substance other than sulphanilamide. Such an X substance has been postulated by Levaditi (1937).

Of the other sulphanilamide derivatives much cannot be said at the moment but the fact that both sulphapyridine and sulphathiozole are effective against streptococcus infection but infinitely more so against pneumococcus would make one believe in the specific action and indeed it is not improbable that different compounds will be found each having a greater effect than the other against a particular organism.

The various views which have been advanced to explain the mechanism of action of these group of drugs may now be discussed. In chemotherapeusis the ideal aimed at is the stimulation of the natural process concerned in the particular infection and at the same time inducing by direct or indirect action on the organism or their environment, such changes as would be conducive to the success of the natural processes at work. How far this ideal has been realised it is difficult to assess at present.

The different views regarding the action of these compounds may be summarised as follows:

1. that they have a stimlating action on the specific and nonspecific body defences;
2. that they neutralise toxic bacterial products;
3. that they act on the bacteria themselves, either as germicides (bacteriolysis), or in some other subtle fashion by interfering with the invasive power or ability to multiply (bacteriostasis); and
4. some combination of two or more of the above.

It can be taken as proved that sulphanilamide in concentrations obtained in the body and tissues of patients has a bacteriostatic as well as bactericidal effect *in vitro*.

Administering sulphanilamide, Hoare (1938) observed that blood may acquire this bactericidal property within an hour or after a longer interval depending on the rate of the absorption of the drug.

He further noted a close relation betwen the bactericidal action on strains of Strepto. hæmolyticus *in vitro* and the reaction of these strains to sulphanilamide treatment *in vivo*—a fact also observed before by Bliss and Long (1937).

It may be noted that sulphanilamide displays a 'lag' phenomenon in their activity, *i.e.*, it is not immediately active either *in vivo* or *in vitro* either as bactericidal or as bacteriostatic. This means that either a new compound is formed as suggested by Mayer which is an oxidation product of sulphanilamide, *viz.*, p-hydroxylaminobenzene sulphonamide, which acts without a latent period or that inanition may be the cause of bacteriostasis as suggested by Whitby. This delayed action indicates that these drugs do not act immediately on the primary inoculum and that although some multiplication of the bacteria occurs during the time that the drug is slowly absorbed for the first six hours, but as absorption progresses multiplication becomes increasingly difficult and eventually ceases.

The fact that the drug is more soluble in fatty capsules of Str. hæmolyticus than in an aqueous solution indicates that as age increases the concentration of sulphanilamide in the fat of each individual organism is likely to increase culminating in bacteriostasis.

McIntosh and Whitby (1939) observed that the time 'lag' before these drugs became effective, indicates that they slowly combine with or neutralise, some food substance or enzyme essential to the activity of the organism. In an abundant medium such as the blood actual food will probably not be destroyed or fixed. They suggest that the drug may inactivate the bacterial enzyme of which this food factor is a substrate.

Earlier, Lockwood (1938) on the basis of the *in vitro* experiments suggests that sulphanilamide prevents the specialised metabolic activity required of the invasive organism by preventing the utilisation of the native protein substance.

Inhibition of capsule formation—This view was originally put forward by Levaditi and his co-workers in connection with streptococcus and pneumococcus.

Whitby (1939) also found that pneumococci continued to multiply in the peritoneal cavity of mice for about four hours after receiving M & B 693 but that soon after this time the organism showed degenerated capsular changes which became swollen and crenated and eventually disappeared. Further work suggests that the nutrition of the organism is affected, probably they become more vulnerable by this process to phagocytic action.

Neutralisation of toxins—The view that sulphanilamide neutralises the hæmolysins and leucocydins has received further confirmation. Nevertheless this view has been strongly criticised by many observers and as matters stand "it seems that the inhibitory action of sulphanilamide on toxin formation is due to the inhibitory effect on the growth of the micro-organisms, and is in fact, an effect caused by many disinfectant substances when present in concentrations sufficient to prevent growth." (Findlay, 1940).

Reticulo-endothelial system—Finklestone *et al* (1937) believed that sulphanilamide stimulates the reticulo-endothelial cells. On the other hand McIntosh and Whitby (1939) have shown that splenectomy has no influence on the protective action of these compounds. Further they failed to find any evidence of stimulation of this system in their numerous experiments in which spleens of animals inoculated with living coccus and protected with M. & B. 693 were examined.

Leucocytes and Phagocytes—Sulphanilamide produces if anything, slight leucopenia and intensive administration of M. & B. 693 in mice produced no change in the leucocytic count, and the fact that the drug has an effect *in vitro* in serum and broth as well as in whole blood seem to negative the idea that leucocytes are a primary necessity for its activity.

The effect on phagocytosis is conflicting, while some observers noted phagocytosis others failed to do so. It has, however, been suggested that a serum sulphanilamide complex is formed which acts as opsonin, rendering the bacteria more phagocytable.

Specific Antibody Formation—McIntosh and Whitby (1939) showed that the quality, quantity and speed of production of immunity produced in animals cured by M. & B. 693 of a living infection seem to be fundamentally the same as that produced by orthodox active immunisation. Further the degree of immunity produced is unrelated to the dose of the drug and is proportional to the number of organisms inoculated as in orthodox active immunisation, being greater when a large number of living cocci are inoculated and smaller with small numbers. This would suggest that the drug has no stimulating effect on the defensive mechanism, nor does it affect the production of recognised specific antibodies.

The mode of action resulting out of these observations may be summarised after McIntosh and Whitby as follows:—

That these drugs do not stimulate leucocytic or phagocytic activity; that they do not affect the speed of production, or the quality or quantity of specific immune bodies; that both *in vivo* and *in vitro*, these drugs are not instantly active ('lag' phenomenon) and that there is a quantitative relationship between the effective dose and the number of bacteria affected; that they are active on highly virulent organisms and those in the logarithmic phase of multiplication; that they are inactive on "rough" organisms; and finally they are not simple germicides. They probably act by neutralisation of some metabolic function or enzymotic activity.

It has been suggested by Cokkinis that they do not help development of immunity, so that when the treatment is stopped there is just the possibility of a relapse. Moreover, by stopping the activity of the infective organisms they may hinder formation of immunity in the body thus leaving the patient with a latent infection without the means to combat it.

These drugs are selective in their action since only certain bacteria are susceptible. It is therefore necessary that the nature of the infecting organisms should be known before administering the remedy. Even susceptible bacteria respond differently to the treatment; while some forms are inhibited by smaller doses for a short period, others require larger doses for a longer period.

Toxic Manifestations

Ehrlich's observation that one must be prepared to run certain risks in order to do effective chemotherapy holds good to-day with regard to these compounds which are liable to give rise to a number of toxic manifestations, the cause of the majority of which is still unknown. These have been provisionally grouped by Findlay (1940) as follows:—

1. Reactions affecting the nervous system—mental disturbances, giddiness, palpitation, headache, "drug fever", sometimes associated with skin rashes, optic neuritis, tinnitus, paræsthesia, peripheral neuritis.

2. Reactions affecting the skin—maculopapular and urticarial rashes, sometimes associated with exposure to light; exfoliative dermatitis.

3. Reactions affecting the hæmopoietic system—leucopenia, agranulocytosis, acute hæmolytic anæmia, thrombocytopenia.

4. Reactions affecting the urogenital system—acute nephritis, urinary irritation, albuminuria, nitrogen retention, partial azospermia (?).

5. Reactions affecting the digestive system—nausea, vomiting, diarrhœa, constipation, toxic hepatitis (?).

6. Reactions affecting pigments—(*a*) cyanosis; (*b*) methæmoglobinæmia; (*c*) sulphæmoglobinæmia; (*d*) excessive porphyrin formation.

But the toxic reactions may be usefully considered under the following categories:—

Mild reactions include headache, vertigo, epistaxis, anorexia, nausea, mild vomiting, general malaise, slight cyanosis and palpitation.

Moderately severe reactions consist of marked and persistent cyanosis, persistent dyspnœa, severe vomiting, diarrhœa, prostration, skin reaction, neuritis, hyperpyrexia or subnormal temperature and acidosis.

Severe reactions are agranulocytosis and hæmolytic anæmia.

In any case of toxic manifestation it is natural to withhold the administration of the drug and to force fluid to help elimination. It is, however, not necessary to withhold the drug in the first group. In the second group one should use his discretion, but in the third group stoppage of the medicament is imperative.

Cyanosis is not an uncommon occurrence and is more unpleasant than grave and can be ignored unless associated with much vomiting, dyspnœa or cardiac failure. It may be due to

1. Presence of a coloured compound of the drug.
2. To methæmoglobin formation (MHb). It is usually transient and disappears within 24 hours and does not necessarily demand stoppage of the drug. Exactly how methæmoglobin is formed is not known.
3. Sulphæmoglobin formation (SHb). This is derived from H_2S absorbed from the gut. It may cause a lavender blue tint and may persist for six weeks after stoppage of the drug.

It has been suggested that an excessive formation of H_2S or the presence of a suitable catalyst would cause the sulphide to combine with the hæmoglobin resulting in the formation of SHb. The role of this catalyst has been ascribed to the sulphanilamide.

Inspite of the fact that sulphonamide-treated patients do not get sulphur or sulphur containing substances yet MHb and SHb still continue to appear. Again many patients with intense cyanosis do not show either of the pigments. It is only by spectroscopic examination that it is possible to differentiate between sulphæmoglobinæmia and methæmoglobinæmia. But in general practice it is not always easy to have this, therefore a working hypothesis is necessary for daily use.

1. Administer methylene blue in 2 gr. doses thrice daily. If cyanosis is due to methæmoglobinæmia it will improve or disappear. In bad cases it is given by injection in doses of 1 mg. per kilo of body weight.
2. Do not stop the drug if it is found necessary.
3. Whenever cyanosis deepens and other symptoms appear stop the administration of all sulphonamide drugs.

Other measures requiring attention will be to stop all foods containing sulphur (eggs, onions, etc.) and to prescribe a low residue diet.

Since derangement of porphyrin metabolism is one of the toxic effects of sulphonamide group of drugs, Nicotinic acid is now being given for the relief of the toxic effects of these drugs on the idea that excessive porphynuria in pellagra disappears with this drug. Dose 30 mg. tablets, B.D. Increased fluidity of the colonic contents favours absorption of H_2S. Therefore start treatment with a colonic wash and avoid all purgatives with the exception of liquid paraffin. Sulphates and other sulphur containing drugs should also be avoided. Drugs of the phenacetin group, in fact any drug derived from aniline or nitrobenzene should be withheld.

In severe cases blood transfusion may be necessary. Oxygen inhalation may be given but is of little value in MHb.

Anæmia—Two types of anæmia may occur, *viz.*,

1. Acute hæmolytic anæmia.
2. Anæmia unassociated with hæmolysis.

Acute hæmolytic anæmia is sudden in onset. In some cases this may be accompanied by varying degrees of jaundice and signs of diminished hepatic function. Or there may be some pyrexia, or there may be leucocytosis, chiefly of the polymorphonuclear type.

Acute hæmolytic anæmia is a serious complication and demands stoppage of the drug, administration of fluid and transfusion of whole blood.

Anæmia unassociated with hæmolysis but with a faint trace of icterus is not a serious complication and improves with stoppage of the drug.

It will, therefore, stand to reason that this drug should be avoided in patients suffering from profound anæmia.

Agranulocytosis is the most serious complication but fortunately rare. It develops after some weeks of treatment, a fact which points to limiting the administration of the drug to a period of not more than a fortnight at a stretch. It is possible that idiosyncrasy plays a large part. As it is marked by diminution of leucocyte a watch should be kept on this and the drug stopped at once as soon as there are signs of leucopenia.

The treatment consists of stoppage of the drug and liberal use of fluids to favour elimination. Transfusion of blood, application of x-rays, parenteral liver have all been tried without much benefit. The only promising form of treatment so far known is the administration of the sodium salts of pentose nucleotides prepared from nucleic acid. This is marketed under the name of Pentnucleotide or Pentide, and is supplied in solution containing 0·7 grm. in 10 c.c. solution. It has

been claimed that the mortality can be reduced with this treatment from more than 70 per cent to approximately 25 per cent by early and intensive treatment. 10-20 c.c. should be injected deep into the gluteal muscle twice daily for the first three days, followed by 10 c.c. once or twice daily for a week. Total white cell and differential count should be made each day. In favourable cases an increase in granular leucocytes occurs usually between the 3rd and 5th days.

Drug fever—A secondary rise of temperature usually seven to eight days after the onset of the drug treatment is sometimes observed. It often subsides with the discontinuance of the drug. It is important to distinguish this fever both from recrudescence of the bacterial infection and from fever associated with drug eruption. This has been ascribed to the liberation of toxin and is allied to anaphylaxis or malaria.

Skin lesions—Various types of skin rashes have been observed. These appear more often with sulphanilamide and sulphathiazole and less with sulphapyridine. They generally appear about the 8th or 9th day, although may be any time within 21 days and are seen chiefly on the exposed surface of the skin, or may be generalised. Urticarial, scarlitiniform, purpuric, maculopapular; exfoliative dermatitis. These are accompanied by itching, œdema, or icterus and disappear with the stoppage of the drug.

Therapeutic Uses

The introduction of the drugs of this group has altered the outlook of many diseases which were not amenable to treatment. Clinical reports are numerous proving the value of these drugs in streptococcal, meningococcal, pneumococcal, gonococcal, bacterium coli and gas gangrene infections; whilst in infections with staphylococcus and Brucellus organisms the reports, though not so dramatic, are encouraging. It should, however, be noted that these drugs have been found more successful, in fact sometimes quite spectacular, in coccal than in bacillary infections. Reports are now available regarding their use in plague, typhoid fever, small pox, trachoma, etc.

It is not possible to discuss here the innumerable diseases in which these drugs are now being used. The good results obtained in streptococcal and pneumococcal infections has led the physicians to use the drugs in all and sundry and some good results are attributed to this drug which are not found justified by more careful observers. Moreover, owing to want of proper knowledge they are often used without any consideration of their untoward effects in doses bordering on toxic. It must, however, be said in defence that unless the drugs were misused the untoward effects could not have been noted and recorded. So that one can always find good coming out of evil.

Streptococcal diseases.—Since the publication of the results of the remarkable beneficial effects of prontosil in puerperal sepsis by Colebrook and Kenny in 1936 the sulphonamides have been successfully tried in a variety of streptococcal infections like puerperal fever, erysipelas, tonsillitis, septic complications of measles, scarlet fever, whooping cough, pyelitis, cellulitis, pneumonia, empyema, etc. Infections with hæmolytic streptococcus Group A are the most vulnerable. Some of these will be briefly considered here.

Puerperal sepsis.—Though the incidence of mortality in this condition has within recent years diminished, due probably to greater attention to hygienic measures and ante-natal care, there cannot be any doubt about the value of these drugs in this condition. One should however, remember, as emphasised by Colebrook (1939) about the small margin of safety between the effective therapeutic dose and the toxic dose. He cites cases which developed agranulocytosis with 60 grms. of the drug, whereas 20-30 grms. are necessary for the effective therapy of a severe case of streptococcal infection. He considers that if a patient does not improve during the first five or six days of treatment, the causal organism is probably not sensitive to the drug. During these first six days, if the patient is improving and fever subsiding, leucocyte count is not necessary, but if the temperature does not fall or if there be any disturbing symptoms such as headache, white cell count should be made every second or third day. Whenever more than 25 grms. are administered, or the treatment is prolonged for more than 10 days, leucocyte count should be made at short intervals.

Apart from septicæmia associated with puerperium these drugs have been used in streptococcal septicæmia unassociated with parturition with good results; and also streptococcal pyelitis associated with pregnancy or not.

Prophylactic Use

Mass prophylaxis of puerperal infection is not a practical proposition inasmuch as any possible prophylactic value is offset by the danger of toxic reaction.

But opinions are unanimous regarding the use of these drugs in all cases where there is undue risk of infection during the puerperium. Similarly these drugs may also be used in surgical cases with risk of infection with streptococcal hæmolyticus. One possible disadvantage has been pointed out by Garrod (1938); he found that previous sulphanilamide treatment by killing or damaging the causal cocci, can render bacteriological diagnosis of any infection which may arise exceedingly difficult.

Erysipelas—These drugs have proved exceedingly useful and in majority of cases the clinical symptoms rapidly disappear. Sulphanilamide—1 grm. every 4 hours until the temperature comes to normal—which takes place between 3 or 4 days; thereafter 1 grm. three times daily for a further period of 14 days.

Children under 2 years—2-3 tablets of 5 grs. daily usually crushed and given with food or drink.

2-5 year—2 tablets of 5 grs. 3 times a day.

6-16 years—3 tablets of 5 grs. 3 times a day.

Pneumonia—Though sulphanilamide was used in pneumonia, the introduction of sulphapyridine has altogether altered the prognosis of this disease and the mortality rate has been considerably reduced. Sulphathiazole is of very recent origin and clinical reports of its use in pneumonia though have not been many yet the results so far obtained are encouraging.

One fact requires to be emphasised. Pneumococcus may develop a toleration or drug fastness to M. & B. 693 when repeated small doses have been used as has been found both experimentally and clinically. It is, therefore, necessary that the initial dose should be large and the immunity of the body should be raised to as high a level as possible by active or passive, specific or non-specific means. In pneumococcal pneumonia when the patient is moderately ill, oral administration of 4 grm. in the first dose is followed by 1 grm. 4 hourly until the patient's temperature remains normal for 48 hours. The dose is then reduced to 1 grm. 6 hourly and is continued later in 0·5 grm. doses until all pulmonary signs are cleared. A total of 40 to 50 tablets (20 to 25 gm.) on a decreasing scale during five days is generally given. In severe cases 0·05 grm. of Sodium sulphapyridine (Dagenan Sodium) per kilo of body weight may be injected in a 5 p.c. solution in sterile distilled water at the rate of 5 c.c. per minute. If 1 grm. of sulphapyridine is being given orally every 4 hours, usually two injections will suffice. The injection may be repeated at intervals of 6 to 8 hours. According to Marshall and Long a blood level of 4 mg. per 100 c.c. is desirable in adults to render the drug effective. For children it can be given crushed and suspended in glucose.

Finland *et al* (1939) after investigations into three series of cases receiving specific serum or sulphapyridine alone and a combination thereof made the following observations:—

(*i*) In the majority of cases when serum alone was used, symptoms abated within 6-24 hours.

(*ii*) When a combination therapy was used, the drug could be omitted 12-36 hours of the first dose and smaller doses of the serum are necessary than without the drug.

(*iii*) When the drug was used alone symptoms were more prolonged and the drug must be continued for a minimum of 48-72 hours after the subsidence of the temperature.

These authors suggest that in all cases of pneumonia blood culture should be done before treatment commences, and further that the treatment of election is to institute sulphapyridine therapy as soon as diagnosis is made, combined with the administration of specific serum at the earliest possible moment.

Meningococcal Meningitis—There is no doubt that early diagnosis and the use of specific serum of increased potency has considerably reduced the mortality rate, yet the sulphonamides have proved their effectiveness beyond any doubt. Uleron, because of the inability to reach the cerebrospinal fluid, in proper concentration, should not naturally have any favourable reception in this disease although Oetken (1938) after successful treatment of two grave cases with large doses of this drug, is of opinion that the good effects are due to the biological relation between meningococci and gonococci. Sulphanilamide though used successfully has, of late, been replaced by sulphapyridine.

Ordinarily the oral route should be the route of choice. Intrathecal administration can only be utilised in refractory cases or in cases where peroral or other parenteral route fail. To prevent recurrence the drug had better be continued for some time after clinical symptoms have abated.

With regard to combined serum and drug treatment, the observations of Banks (1938) are of interest.

He thinks sulphanilamide a very efficient form of treatment in both group I and group II infections. The initial dose should be high, and the concentration in the cerebrospinal fluid should be 5 mg. per 100 c.c. within 24 hours and should be maintained for three days. Combined drug and serum treatment is very effective, specially in severe cases in both group I and group II infections.

Gonorrhœa—The group of drugs has reduced both the duration of the illness and the incidence of complications to a very great extent. In the treatment of this disease several factors require careful consideration, *viz.*,

(*i*) suitable time for commencing treatment,
(*ii*) suitable preparation to be used,
(*iii*) the dosage and duration of treatment,
(*iv*) period of observation, chances of relapse,
(*v*) value of ancillary measures.

Most observers agree that it is desirable to wait until the eighth day or longer before beginning treatment with Uleron, sulphanilamide or Albucid, whilst those who use sulphapyridine prefer not to wait.

The drugs mentioned are generally used but sulphapyridine has practically replaced the others since it can be used in all types of cases and in any stage of the disease. It acts with greater rapidity in early acute cases, the discharge diminishes and the gonococci disappear in about three days. In chronic cases more prolonged treatment, or repeated short courses with local antiseptics, *e.g.*, urethral irrigation is required.

Uleron. Its use is favoured in chronic cases. It should be used with caution as excessive doses may cause peripheral neuritis. Irrigation is given till the tenth day of the infection. The dose is 3 grm. daily for four days or 4 grm. daily for three days. If the slide is still positive, the treatment is repeated after an interval of 8 days. If necessary a third course may be given after the same period of interval. But not more than three courses should be given.

Albucid. It is used extensively in Germany. It is better tolerated than Uleron and produces few toxic manifestations. First week, urethral irrigation thrice daily and injection of vaccine. Second week, 3 tablets (1·5 grm.) three times a day along with irrigation. Third week, no treatment unless discharge continues when irrigation only should be used. Fourth week, tests for cure are started if the discharge ceased at the end of 1st week, if not the course should be repeated, 1st day, 5; 2nd day, 4; 3rd day, 3; 4th day, 2 tablets—three times a day.

Sulphapyridine. Two tablets each of 0·5 grm. should be given three times a day for five days as a minimum course. These are given every four hours commencing at 8 A.M. As a rule no toxic effects are observed though some patients may complain of nausea which is relieved by alkalies. If vomiting is present the soluble sodium salt may be given by intramuscular injection, subcutaneous injection causes necrosis. The treatment should not be more than ten days at a time. If another course is necessary it should be after an interval of one week. It has been used with success in gonorrhœal ophthalmia.

Women can tolerate the drug well. A small percentage fails to respond to this treatment. If after three courses the cure is not effected or there is relapse search must be made for some deep-seated or enclosed focus of infection.

Infection of the urinary tract with other bacteria—The introduction of the sulphonamide group of drugs has given the practitioner a new and potent means of combating infections of the urinary tract. They are used in acute, subacute or chronic cases, both in adults and children, and in pyelitis of pregnant women. Choice of preparation, however, falls on sulphapyridine. These drugs are almost wholly excreted in the urine in effective concentration (20-40 mg. per 100 c.c. of urine). They also act best in neutral or alkaline medium (pH between 7-8) though their activity is not lost over a wide range of pH (5-8). These preparations may be used alone but act better if the treatment is combined with alkalies. The beneficial effects of diuresis and of alkalies need not be sacrificed while the additional antibactericidal action of sulphonamides helps to reduce the time required for the sterilisation of the urine. It is generally given in 7½ gr. tablets four times a day. With this combined treatment there is rapid diminution of fever and toxæmia, and with the disappearance of pus from the urine which takes about one week to ten days the urine in culture becomes sterile.

Some observers, however, consider sulphonamides as more toxic than mandelic acid and in operation cases prostration, gastric irritation and cyanosis are undesirable. It is specially effective in B. coli, Prot. vulgaris, B. ærogenes, but less effective in Staph. aureus and practically inert in Str. fæcalis.

The above is not an exhaustive survey of the diseases in which these drugs are used some with success and in others as an experimental measure. A passing reference may be made of a few others only.

They have been found very effective in the treatment of chancroid in 4 grm. doses daily for seven days. They are worth a trial in ulcerative endocarditis when due to various pyogenic cocci. Similarly they are useful in acute tonsillitis when the general infection is very marked. They are also used in diseases of the middle ear at the beginning of illness.

They have been used in ophthalmic practice with benefit particularly in acute conjunctivitis, specially gonococcal conjunctivitis, corneal ulcers of all types, intra-ocular infections, iritis and panophthalmia and trachoma.

Local Application

These drugs, at least some of them have been used locally and has given satisfactory results in some cases. In bronchitis or bronchiectasis inhalation of the soluble prontosil (10 c.c. of 2-5% solution) by means of a spray has been used with success.

Direct injection into tonsillar abscess or topical administration in erysipelas or in urinary infections, has been used, it is stated, with success.

Different Compounds Compared

Sulphanilamide.—Absorbed within four hours though there is variation in different individuals. It is completely excreted within 24 hours in both as free and conjugated acetylated inert form. Excretion is delayed in renal damage. Effect of one dose persists for six hours. It should, therefore, be administered every 4 to 6 hours. In man 3 gm. daily may produce toxic symptoms. Central nervous degenerative changes have not been seen in man, at least so far not recorded. Slight acidosis is produced but overcome by alkalies. SHb and MHb with cyanosis may occur. Hæmoglobinuria has been recorded by Lockwood *at el.* Specially useful in actute streptococcal infections, septicæmia, erysipelas. For meningococcal meningitis it is better than sulphamidochrysoidin and prontosil sol. It is effective in B. coli and Prot. vulgaris, ineffective against Str. fæcalis and group D B hæmolytic streptococci. Successful uses claimed in undulent fever, actinomycosis, malaria and plague.

Sulphamidochrysoidin and Prontosil soluble—The former is almost obsolete and is of historical interest. Prontosil soluble is useful when administration by the mouth is not possible and immediate result is necessary. Dagenan Solution may be used by preference.

Proseptasine and Soluseptasine—As compared with sulphanilamide, proseptasine is less toxic. Not much is known of its concentration in the blood or other fluids and it is not known if the less toxicity is due to slow absorption owing to insolubility. Clinically it is useful in all conditions where sulphanilamide is used. For its alleged safety it can be used in cases of less severe hæmolytic streptococcal infections. The same remark applies to Soluseptasine.

Ulcron is not broken down to sulphanilamide and is effective against staphylococcal infections of mice and rabbits. It is the most widely used remedy in Germany for gonorrhœa but it is more toxic than sulphanilamide. It has often caused polyneuritis.

M. & B. 693—It has the advantage of being highly active against pneumococcus of several types and also more powerful against Str. hæmolyticus than sulphanilamide. It has been used with some success in bubonic plague and influenzal meningitis after sulphanilamide has failed. It has been used sometimes with brilliant results in staphylococcal infections.

It is supposed to be extremely nontoxic and has no action on blood and does not cause porphyrinuria in animal experiments, in doses sixteen times the effective curative dose.

Despite its relative insolubility it is rapidly absorbed, and Whitley thinks more rapidly than sulphanilamide. It, however, leaves the gut more rapidly and is more slowly excreted. Some 50 p.c. is detoxicated as acetyl compound.

Nausea and vomiting may preclude its use. Vomiting has been ascribed to local irritation in a sensitive stomach and to a certain extent central. In most cases giving the drug in divided doses in smaller amounts and more frequently will obviate the trouble or the sodium salt (Dagenan Sodium or M. & B. 693 Soluble) which is obtained in 33 1/3% aqueous solution in 3 c.c. ampoules may be used by intramuscular injection. Several cases of hæmaturia have been recorded. This is possibly due to damage to the kidney tissue by sharp crystals of urinary calculi.

Sulphathiozole—It is very quickly absorbed and equally quickly eliminated, therefore toxic effects are less likely to occur though hæmaturia is observed. Rapid elimination implies frequent administration, in fact more frequently than others. It has been found to be of special value in plague at the Haffkine Institute in the

hands of Sokhey and Dikshit both in experimentally infected mice and clinically in field work at Bihar. This preparation appears to be a further improvement and may possibly supplant others.

REFERENCES

BANKS (1938)—*Lancet*, 2: 7.
BLISS AND LONG (1937)—*New England J. Med.*, 217: 18.
COLEBROOK (1939)—*Lancet*, 2: 158.
FINDLAY (1940 a)—Recent Advances in Chemotherapy, Second Edition. p. 266-267.
Idem (1940 b)—*Ibid*, p. 458.
Idem (1940 c)—*Ibid*, p. 429.
FINKLESTONE-SAYLISS, PAIN & PATRIC (1937)—*Lancet*, 2: 792.
FINLAND, SPRING, LOWEL AND BROWN (1939)—*Ann. Int. Med.*, 12: 1816.
GARROD (1938)—*Lancet*, 1: 1125 & 1178.
HOARE (1938)—*Ibid*, 1: 635.
LEVADITI (1937)—Quoted by Findlay (1940)—p. 452.
LOCKWOOD (1938)—*J. Immunol.*, 35: 155.
MAYER (1937)—Quoted by Mashall, Jr. (1939) *Physiol. Rev.*, 19: 240.
MCINTOSH AND WHITBY (1939)—*Lancet*, 1: 431.
OAKLEY (1937)—*Biochem. J.*, 31: 729.
OETKEN (1938)—*Deutsche med. Wchnschr.*, 64: 1683.
WHITBY (1937)—*Lancet*, 1: 1517.
Idem (1938)—*Ibid*, 1: 1210.

LESIONS OF THE OPTIC NERVE IN VITAMIN B_1 DEFICIENCY

T. K. RAMAN, M.D., D.T.M. (Cal.)
and
C. ABBU, M.B. & C.M., D.O.M.S. (Lond.)
Andhra Medical College and King George Hospital, Vizagapatam.

Kono (1895) reported six cases of beriberi with amblyopia, central scotoma, and contraction of the visual field without any changes in the fundus. Yamamoto (1903) observed some cases in which there was no change in the fundus, some with partial atrophy of the papilla restricted to the temporal half and others in which there was complete optic atrophy. Ichihara (1903) observed transitory contractions of the outer fibres of the optic nerve in five cases of kakke-scotoma (quoted by Elliot and Miyashta, 1920).

Shastid (1929) reported two cases of optic neuritis of apparently unknown origin cured by large doses of vitamin B. In one case wheat germ extract (vitavose) and in the other yeast was used.

Moore (1934) described 12 cases of avitaminosis with retrobulbar neuritis and partial optic atrophy, 9 of which responded to treatment. He concluded that deficiency or toxic deficiency was responsible for these signs. In 1937, he confirmed his previous findings and concluded that the condition of the optic nerve was a partial post-optic atrophy following retrobulbar neuritis.

Moore and Woods (1940) in discussing the pathogenesis of syphilitic primary optic atrophy, put forward the theory that optic atrophy may be due to a combination of neurosyphilis and vitamin B_1 deficiency.

The present series includes 34 cases in which the lesions of the optic nerve were investigated. The clinical conditions are classified under the following heads—

1. Beriberi group of diseases:

(*a*) Beriberi. In this condition there is œdema, cardiovascular disturbance and peripheral neuritis (15 cases).

(*b*) Toxic peripheral neuritis. There is no œdema but tachycardia and peripheral neuritis are present (2 cases).

(*c*) Avitaminosis B_1. Peripheral neuritis alone is present; cardiovascular disturbance and œdema are absent (4 cases).

2. Pellagra (10 cases).
3. Beriberi combined with pellagra (1 case).
4. Diabetes mellitus (2 cases).

SUMMARY OF NINE CASES

1. Beriberi with contraction of field of vision.

Case No. 1. P. P., a Hindu male aged 48 years, was admitted on 10. 3. 40 with a history of recurrent beriberi.

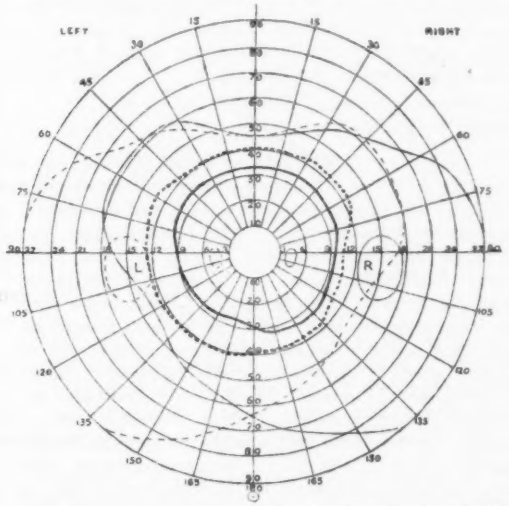


Fig. 1. A case of beriberi (No. 1) showing definite concentric contraction of field of vision of both eyes, right more than the left. Test object: size 1 mm., colour white.

The first attack occurred three years previously. Physical examination: A fairly nourished individual with œdema of the legs and feet, heart slightly enlarged with systolic murmur in the mitral area. Blood pressure: 112/78. Nervous system: subjective sensation of tingling and numbness in the hands and feet, sensations normal, deep reflexes lost both in upper and lower extremities. Other systems were normal. Eyes: concentric contraction of the field of vision in both eyes. (Fig. 1). He was discharged relieved of his symptoms on 23.3.40.

Case No. 2. C. J., Hindu male aged 3 years, was admitted on 2. 6. 40 with a history of œdema of the legs, tingling and numbness of the lower extremities and difficulty in breathing of six months' duration. Ten years previously he had an attack of beriberi in Rangoon which lasted for 3 months. Physical examination: A moderately nourished individual with slight anæmia, with toxæmia, paraplegia, wrist drop and general anasarca. Circulatory system: heart rapid beat (120 per minute), enlarged with systolic murmur in the mitral and pulmonary areas. B. P. 110/10. Nervous system: cranial nerves normal except the second, anæsthesia of hands and feet; complete motor paralysis with wrist drop, deep reflexes lost both in the upper and lower extremities, plantar response extensor, abdominal reflex present and calf muscles tender. Urine: normal. Fundus examination showed a streak of hæmorrhage on the temporal margin of the right optic disc just at the middle line, and two small patches of exudate on the superior and inferior margins of the left optic disc.

He was given 2 c.c. of liver extract every alternate day for seven days. The toxic symptoms disappeared and œdema was considerably reduced. After a few days on yeast all the signs and symptoms disappeared except peripheral neuritis. Blood pressure rose to 110/90. Lumbar puncture on 28. 8. 40 showed normal C. S. F. W. R. doubtful in blood but strongly positive in C. S. F. Eyes: (12. 8. 40) field of vision practically normal; (25. 9. 40) vision 6/9 in both eyes, concentric concentration of field of vision in both eyes. He was discharged on 5. 10. 40 completely cured.

Cace No. 3. V. S., Hindu male aged 25 years, was admitted on 19. 10. 40 with a history of recurrent attacks of dysentery for 3 years and œdema and tingling and numbness during the previous three months. Physical examination: A fairly nourished individual with slight angular stomatitis. Nervous system: intelligence normal, cranial nerves normal except the second; gait ataxic, anæsthesia of the hands below the elbow and legs below the knee; deep reflexes lost, plantar response flexor and calf muscles tender. Other systems were normal. Motions showed slight mucus with Charcot-Leyden crystals indicating an old amœbic infection. Agglutination of blood against dysenteric organisms: Shiga 1 in 160, Flexner 1 in 80 positive. Cerebrospinal fluid normal with negative Wassermann reaction. Eyes (12. 10. 40): vision 6/6 both eyes, fields definitely contracted concentrically in both eyes. (Fig. 2) He was treated with codliver oil, yeast and vitamin B_1 injections on alternate days from 22. 10. 40. His general condition improved and he was able to walk at the end of a month. A second examination on 11. 11. 40 showed a normal field of vision.

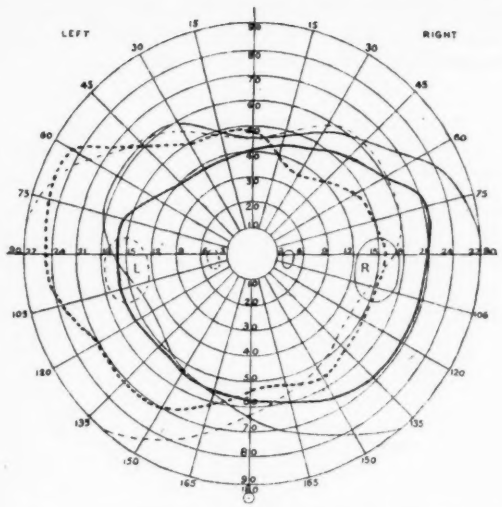


Fig. 2. A case of beriberi with mixed amœbic and bacillary dysentery (No. 3) showing slight concentric contraction of field of vision of both eyes, right more than the left. Test object: size 1 mm., colour white.

2. *Beriberi with normal field of vision.*

Seven cases of beriberi in different stages of the disease showed a normal field of vision and normal *fundus*. A case described. A small boy of 15 years was admitted with symptoms of chronic malaria (B.T.), tachycardia and advanced peripheral neuritis with wrist drop of one month's duration. His œdema disappeared only a few days before admission. Examination of eyes showed normal field of vision and normal fundus. In spite of the advanced peripheral neuritis his optic nerve remained free. He was discharged cured at the end of two months.

3. *Toxic peripheral neuritis.*

A boy of 15 years was admitted with symptoms of toxic peripheral neuritis, dysenteric in origin, in which the field of vision was normal. Agglutination against dysenteric organisms showed Shiga positive 1 in 160, Flexner positive 1 in 320. He was discharged practically cured of his peripheral neuritis after treatment with codliver oil and yeast. Another patient, a Hindu male aged 30 years, admitted with a history of tingling and numbness and inability to use the lower extremities of twenty days' duration showed peripheral neuritis, probably due to an unknown toxin, tachycardia and normal field of vision.

4. *Avitaminosis B_1.*

Case No. 4. C. V. Hindu male aged 25 years was admitted on 14. 10. 37 with a history of dimness of vision and tingling and numbness of the hands and feet of 6 months' duration. Physical examination: A moderately nourished individual with bad teeth and oro-genital syndrome. Nervous system: intelligence normal, all cranial nerves normal except the second, gait ataxic, sensation to cotton wool lost both in upper and lower extremities; biceps, triceps, supinator, knee and ankle jerks lost; plantar response flexor and abdominal reflex present. Cerebrospinal fluid normal. W. R. negative both in blood and C. S. F. Other systems were normal. X-ray of skull showed no evidence of pituitary tumour. Eyes: vision, fingers at half meter distance, both the discs showed evidence of primary optic atrophy. Field of vision practically nil (Fig. 3). He was treated with codliver oil, milk and bread diet and was discharged on 9. 11. 37 without any improvement of his condition.

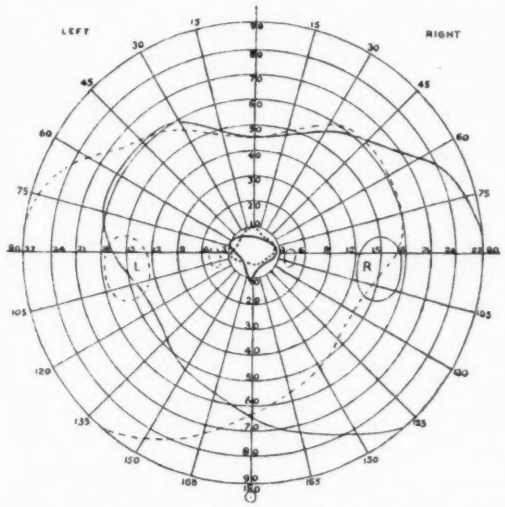


Fig. 3. A case of avitaminosis B_1 (No. 4) showing the smallest field of vision, and ophthalmoscopic examination showed primary optic atrophy. Test object: size 1 mm., colour white.

5. *Pellagra with contraction of field of vision.*

Case No. 5. C. C. Hindu male aged 50 years was admitted on 27. 1. 40 with tingling and numbness of the hands and feet of eight months' duration. The black patches over both the hands and feet were observed only about 10 days previously. Physical examination: Dermatitis, typical of pellagra, was present over the dorsum of the hands and feet. There were atherosclerotic changes in the heart, slight rise of blood pressure (176/115) and symptoms of peripheral neuritis. Cerebrospinal fluid: normal. W. R. negative both in blood and C. S. F. Examination of eyes on 14. 2. 40 showed waxy white optic discs with a slight contraction of the field of vision. A second examination on 26. 3. 40 showed the same condition. He was discharged cured of pellagra but with slight symptoms of peripheral neuritis persisting. He was readmitted on 28. 4. 40 with mild symptoms of pellagra, and definite symptoms of peripheral neuritis. Field of vision on 7. 9. 40 showed still further concentric contraction. Biochemistry of blood and urine: nicotinic acid in blood 0·196 mg. per 100 c.c. nicotinic acid in urine: 0·52 mg.; B. B. S. in urine 17·16 mg. per 100 c.c. The patient gradually recovered with liberal diet, codliver oil and yeast by mouth, liver extract injections and was discharged cured on 19. 10. 40.

Case No. 6. U. A., Hindu male aged 40 years, was admitted on 6. 5 39 for tingling and numbness and inability to walk for the last three months. Physical examination revealed the case to be one of peripheral neuritis. Lumbar puncture showed normal cerebrospinal fluid, without any change in colloidal gold reaction. W. R. negative both in blood and C. S. F. He was given vitamin B_1 (Betaxin) injections, codliver oil and yeast by mouth and a liberal diet and discharged practically cured on 19. 7. 39. He was readmitted on 15. 2. 40 with advanced pellagra and peripheral neuritis. Examination of eyes on 19. 2. 40: vision fingers at two meters distance in both eyes, with primary optic atrophy of both optic discs. He was given liver extract injections and a liberal diet. The condition gradually improved and when he was able to sit up, the

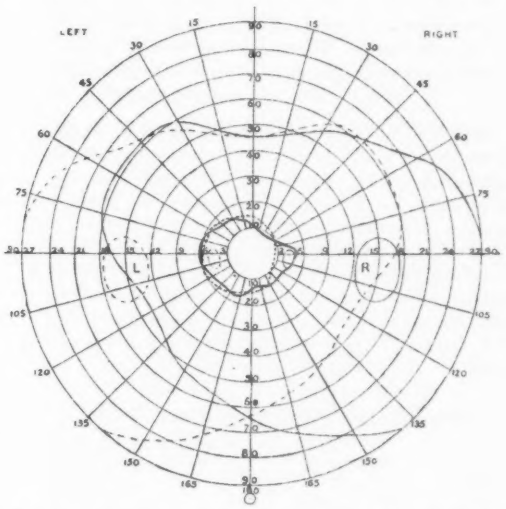


Fig. 4. A case of advanced pellagra (No. 6) with marked symptoms of peripheral neuritis showing definite concentric contraction of field of vision of both eyes. Ophthalmoscopic examination showed primary optic atrophy. Test object: size 1 mm., colour white.

field of vision on 4. 6. 40 showed an advanced condition of concentric contraction in both eyes (Fig. 4). Two months later after treatment with codliver oil, yeast and a liberal diet all the peripheral neuritic symptoms disappeared and examination of eyes on 21. 8. 40 showed vision (R. E.) 6/24; (L. E.) 6/36 improved with glasses to 6/12 and 6/9 respec-

tively. The fields of vision became practically normal. (Fig. 5). He was discharged cured on 21. 8. 40.

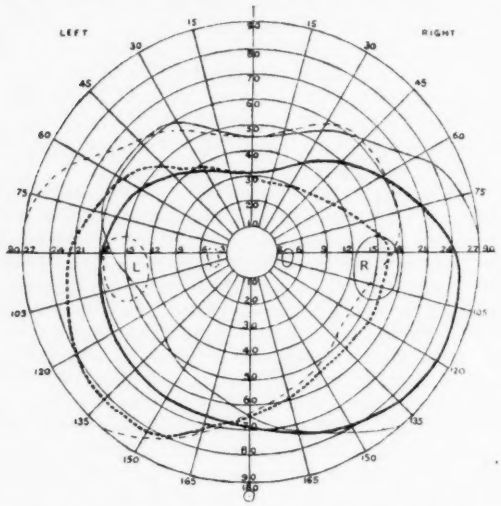


Fig. 5. The same case as above showing definite improvement in the field of vision at the end of two and half months after treatment with a liberal diet, yeast by mouth and the liver extract injections. Test object: size 1 mm., colour white.

Case No. 7. A. V., Hindu male aged 31 years, was admitted on 18. 9. 40 with a history of tingling and numbness and slight œdema of the feet of ten years, and dermatitis of one year's duration. Physical examination: A thin emaciated individual with slight œdema of the hands and feet. Dermatitis was present over the face, neck, hands and feet, an advanced condition of pellagra. Nervous system: subjective sensations of tingling and numbness were present in both the limbs, sensations normal, knee jerks sluggish and plantar response flexor. Blood examination showed picture of microcytic anæmia. Eyes: vision (R. E.) 6/10, (L. E.) 6/5 slight concentric contraction of fields of vision of both eyes. Blood B. B. S. 2·75 mg.; urine B. B. S. 22 mg., nicotinic acid 0·16 mg. per 100 c.c. He was treated with liver extract and nicotinic acid injections, and a liberal diet with milk, bread and eggs. A second examination on 19. 11. 40 showed normal field of vision.

Case No. 8. K. A., Hindu male aged 45 years, was admitted on 5. 2. 40 with a history of dark patches over the back of the hands and feet, and tingling and numbness of the upper and lower extremities of five months' duration. Physical examination revealed signs of pulmonary tuberculosis, pellagra and mild signs and symptoms of peripheral neuritis. Sputum showed tubercle bacilli. Lumbar puncture showed normal cerebrospinal fluid. W. R. negative both in blood and C. S. F. He was running a temperature between 99 and 102°F. Eyes: (R. E.) fingers at 2 meters, (L. E.) fingers 3 metres distance. There was temporal pallor of both the optic discs with definite concentric contraction of field of vision of both eyes (Fig. 6). He was given a liberal diet, codliver oil and yeast by mouth and was discharged on 10. 4. 40 cured of the derma-

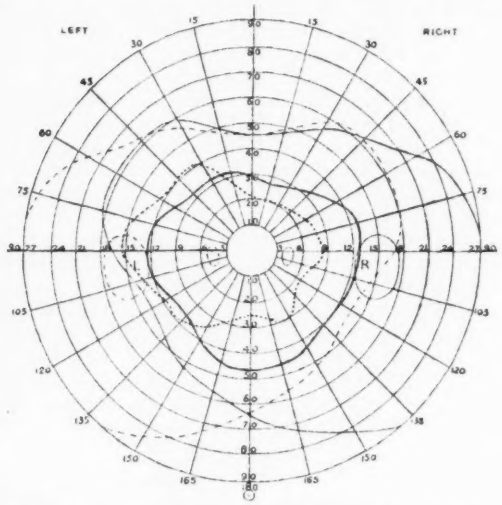


Fig. 6. A case of secondary pellagra (No. 8) with pulmonary tuberculosis and symptoms of peripheral neuritis. Test object: size 1 mm., colour white.

titis but relieved of other symptoms. Examination of the eyes at the time of discharge showed better vision but the fields were not taken.

6. Pellagra with normal field of vision.

Three early cases, and one advanced case with mental symptoms without any evidence of peripheral neuritis showed normal fundus and normal field of vision.

7. Beriberi and Pellagra.

A case of beriberi with pellagra and acute bacillary dysentery showed concentric contraction of field of vision of both eyes. A second examination at the end of one month and a half showed still further contraction.

8. Diabetes mellitus.

Diabetes with peripheral neuritis and contraction of field of vision.

Case No. 9. T. M., Hindu male aged 50 years was admitted on 14. 3. 40 with a history of polyuria, and tingling and numbness of both the upper and lower extremities of one year's duration. Physical examination showed a thin emaciated individual with signs and symptoms of advanced peripheral neuritis. Urine: specific gravity 1042, acid in reaction, sugar

present in large quantities, no albumin. Glucose tolerance test:

		Urine sugar
Blood sugar before glucose:	.. 264 mg.	++
½ hour after ..	.. 280 „	++
1 hour after ..	.. 345 „	++
1½ hours after ..	.. 351 „	++
2 hours after ..	.. 328 „	++

A fairly advanced case of diabetes without any acetone in the urine. Examination of eyes on 15. 3. 40: vision 6/60 both eyes, definite concentric contraction of fields of vision of both eyes more marked in the right eye (Fig. 7). He was discharged on 25. 5. 40.

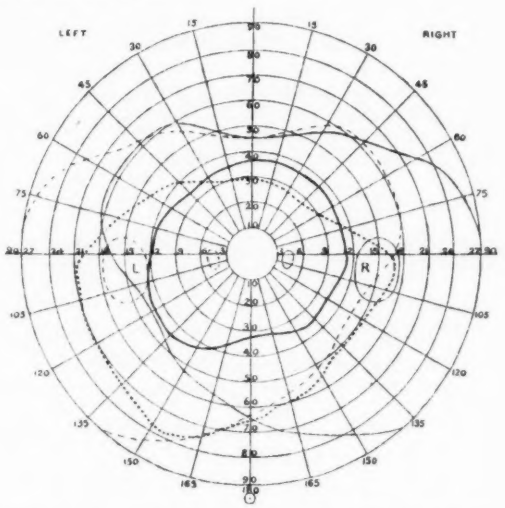


Fig. 7. A case of diabetic peripheral neuritis (No. 9) showing definite concentric contraction of field of vision of both eyes, right more than the left. Test object: size 1 mm., colour white.

9. Diabetic peripheral neuritis with normal field of vision.

The second case was one of advanced diabetes mellitus with peripheral neuritis, first localised in the right arm, then generalised, showing normal field of vision.

Discussion

The name "beriberi group of diseases" has been given to bring together the three clinical entities *viz.*, beriberi, toxic peripheral neuritis and avitaminosis B_1, that can very easily be distinguished clinically at the bedside. The term beriberi has been restricted to the first group clinically characterised by œdema, cardiovascular disturbance and peripheral neuritis.

McCarrison (1928) from experiments on pigeons concluded that "A condition—beriberi columbarum—having all the pathological characters of human beriberi has been produced under experimental conditions in pigeons by means of diets of similar composition to those in use by human sufferers from the disease. The condition differs from polyneuritis columbarum in certain regards of which hypertrophy of the heart is the chief." Megaw (1927) clinically distinguished beriberi from avitaminosis B or polyneuritis avitaminosis. Mahadevan and Raman (1930) also distinguished clinically avitaminosis B from beriberi and reported four cases.

We came across the first case of optic nerve involvement in 1937 in a case of avitaminosis B_1 (No. 4) with complete loss of vision and primary optic atrophy of both eyes.

A considerable amount of work on changes in the eye in beriberi has been done in Japan. Kamath (1911) noted slight haziness of perception in four of his patients and all of them recovered in a fortnight. In this series, the severity of the changes in the optic nerve did not run parallel with the involvement of the peripheral nerves. Different grades of contraction were met with (1) contraction of field of vision of the temporal side (2) slight concentric contraction and (3) definite concentric contraction of the fields of vision. In some cases, fields became still further contracted even though the peripheral neuritis improved. Three cases showed definite improvement after treatment with a liberal diet and yeast and codliver oil by mouth. Injections of vitamin B_1 were given to some patients in addition. Slight differences in the fields of the two eyes could be seen, and in one case the improvement occurred in one eye only. An advanced case of beriberi with wrist drop showed normal field of vision. One case showed hæmorrhages in the retina.

In both cases of toxic peripheral neuritis no change occurred in the fields of vision.

All the four cases of avitaminosis B_1 showed changes in the optic nerve, and one case (No. 4.) showed primary optic atrophy. Here also lesions of the optic nerve did not run parallel with the lesions of the peripheral nerves.

Six cases of pellagra showed varying degrees of contraction of the fields of vision finally leading to primary optic atrophy. Except for the one case associated with pulmonary tuberculosis and another with beriberi all were cases of primary pellagra. In all these cases changes in the field of vision occurred only where there was an associated vitamin B_1 deficiency. Two

cases showed still further contraction of the field of vision at the end of 3 to 6 weeks. In two cases the fields improved after treatment for pellagra and associated vitamin B_1 deficiency. In the case No. 6 showing primary optic atrophy the improvement in the field of vision was remarkable. One case showed pallor of the temporal side of the optic disc but with normal field of vision. Symptoms of peripheral neuritis were absent in the four cases that showed normal field of vision.

In both cases of diabetes mellitus symptoms of peripheral neuritis were present, but only one case showed contraction of the field of vision.

Epidemic dropsy has been omitted from this discussion although cases were seen in Vizagapatam either indigenous or imported. The condition of the optic nerves were not investigated in these cases.

Hughes Lienhardt and Audel (1929) and later Mellanby (1934) observed degenerative changes in the optic nerve in experimental animals fed on a diet deficient in vitamin A. Fazio (1935) was not able to find any changes in the optic nerve in twelve pigeons fed on a diet deficient in vitamin B_1 although changes were seen in the sciatic nerves. The results of experiments on animals are contradictory and in all probability deficiency of both vitamin A and B produces changes in the optic nerve finally leading to primary optic atrophy (Moore and Woods *loc cit*).

Summary

(1) The condition of the optic nerve was investigated in 34 cases. Twenty cases (59 per cent) showed evidence of optic nerve involvement.

(2) Three cases of beriberi and two cases of pellagra showed a slight concentric contraction; five cases of beriberi, two of avitaminosis B_1 four of pellagra, one of beriberi with pellagra, and one case of diabetes mellitus showed definite concentric contraction of the field of vision.

(3) Pallor of the temporal side of the optic disc was observed in one case of beriberi and one of pellagra.

(4) Primary optic atrophy was seen in two cases, one of pellagra and one of avitaminosis B_1.

(5) There seems to be no correlation between the symptoms of peripheral neuritis and the lesion of the optic nerve.

(6) Improvement in the fields of vision occurred after treatment with a liberal diet and vitamin B_1 in five cases.

Acknowledgements

Our thanks are due to all the medical officers of the Medical and Ophthalmic Departments of the King George Hospital for their kind co-operation in carrying on this investigation.

References

Elliot and Miyastha (1920)—*Tropical Ophthalmology.* Published by Oxford Medical Publications. London, p. 405.

Kamath (1911)—Thesis for M. D., University of Madras.

Mahadevan and Raman (1930)—*Indian M. Gaz.*, 65: 355.

Megaw (1921)—Transactions of the 7th Congress of Far Eastern Association of Tropical Medicine. 3: 359.

McCarrison (1928)—*Indian J. M. Research*, 10: 57.

Moore and Woods (1940)—*Am. J. Ophth.*, 23: 4.

Moore (1934)—*Ann. Trop. Med.*, 28: 295.

Idem. (1937)—*Lancet*, 1: 1225.

Shastid (1929)—*Am. J. Ophth.*, 12: 903.

MENSTRUAL DISTURBANCES AND THE A. O. VACCINE

BASHESHARLAL KAPUR, M.D. (Berlin),
Hony. Medical Superintendent,
Lahore Maternity Hospital, Lahore

The common complaints of the patients attending the out door of maternity clinics are the menstrual disturbances, *viz.*, dysmenorrhœa, amenorrhœa, metromenorrhagia, oligomenorrhœa and delayed menstruation. These disturbances are just the symptoms. The cause of the trouble lies some where else. On investigation one finds that the causes can be:—

(*a*) constitutional faults, (*b*) psychoneurosis, (*c*) allergy, (*d*) hormonal defects, (*e*) hypoinsulinism (Liegner) and (*f*) inflammatory troubles.

I would limit my remarks to the inflammatory troubles only. The inflammations are due to pathogenic organisms, which are divided into two groups:

1. Staphylococi, streptococi, B. coli, Neisser's bacilli, etc., and 2. tubercle bacilli.

The effects of the micro-organisms have not been dealt with here.

Tuberculous affection usually points to pulmonary involvement. In lung cases the menstruation is deranged on account of the toxin of the tubercle bacillus; tunica albuginea becomes thicker, the follicle comes eventually to an atresia. Dysmenorrhœa has been described in 42 and amenorrhœa in 17·4 per cent of cases.

But these are not the cases that come under our observation. We get quite healthy-looking women complaining of some menstrual disorder or other. Dysmenorrhœa and oligomenorrhœa are very common. A few have delayed menstruation. As far as metromenorrhagia is concerned, only 3 cases came in our observation. On going deep into the history, patients complained occasionally of a heat sensation in the evening, but the thermometer was not applied.

Many of them have a slight rise of temperature a day or two before or during menstruation. Some begin to lose weight. Leucorrhœa becomes a very prominent symptom.

They knock the doors of *dais* and other quacks for the vaginal discharge and keep on taking quack medicines uselessly until they consult a specialist who investigates the root cause of the trouble. Some of them complained of primary or secondary sterility.

According to Mayer (1933), women with appearance of beard, hair over the nipples and sexual deficiency are more inclined towards tuberculosis.

In our cases none of the above signs were present. They had asthenic build and some of them had hypoplastic genital organs.

On examination of the lungs even radiologically nothing abnormal was detected; per vaginal examination, there was a slight thickening of the adnexæ. In our three cases of metro-menorrhagia the uterus was slightly enlarged. On biopsy curettage tuberculosis of endometrium was detected. In some of the cases with delayed and scanty menstruation (Kapur and Sarojini, 1940) inflammatory tumors of the Fallopian tubes were palpable. Some of the cases of genital tuberculosis are detected incidental to surgical operation (Kapur and Kaul, 1939; Heldt, 1934).

The tubercle bacillus reaches the adnexæ through the respiratory tract and the spread is blood-borne. According to Weibel, peritoneal and genital tuberculosis can exist side by side but it is less common. The Fallopian tubes can get affected directly from the peritoneum.

Diagnosis

Heldt suggests that Besredk reaction should be done. It lies in the guinea pig inoculation with the exudate obtained by the puncture of the pouch of Douglas. Livschina injects gonococci, streptococci and staphylococci and bacilli coli vaccine intracervically and watches the reaction. The negative cases are supposed to be tuberculous.

In 1932, Yoshida described a test, whose underlying principle is that, only when the A. O. recipient is tuberculous, the injection produces a decrease in the number of leucocytes.

A. O. Vaccine

The A. O. Vaccine is prepared from tubercle bacilli of human type. These organisms are deprived of their germinative quality by artificial treatment and yet are left in possession of immunising power as fully as when alive and untreated.

They are kept in physiological salt solution and are placed in a refrigerator for about 4 years. By this process growth and multiplication are not possible because the bacilli are completely deprived of nutrition and warmth and yet they do not decompose. But these bacilli retain their immunity working power.

Method of Yoshida's Test:—The examination should be conducted on empty stomach in the morning. The patient should be at absolute rest. Two examinations of leucocytes should be conducted, first 15 minutes before and the second immediately before the A. O. vaccine injection. The mean is taken of both the counts. The A. O. vaccine is injected at the rate of 1 c.c. per 50 Kgs. of corporal weight. Then 4 half hourly leucocytic counts are done.

The test requires certain precautions:—

1. All the counts should be done by one person.
2. The leucocytic pipettes should be absolutely dry, so that the red ball moves freely in the bulb.
3. If possible self sucking pipettes should be used.

Reading of the test:—1. The test is strong positive when the decrease of leucocytes in one cubic millimeter of blood reaches 2000-3000 and remains at this low figure within two hours after the injection.

2. The test is middle positive when the decrease of the leucocytes is 2000-3000 and reverts to original or increases a little within two hours or when the decrease is 1000-2000 and remains decreased.

3. The test is weak positive when the decrease of leucocytes is 1000-2000 and goes back near the original number within two hours after the injection or when the decrease is less than 1000 and does not return to original.

The Yoshida's test has been done on a very large scale in Japan and other countries and is found to be quite reliable. But to the greatest surprise of Kapur and Sarojini (1940) it was negative in a case where they found tuberculous salpingitis on laparotomy. In another case they found disseminated tuberculosis of the intestines incidental to laparotomy and Yoshida's test was practically negative. It would be essential to investigate the reliability of the test in a large number of cases by controlling the results with these laparotomies on suitable cases.

Case Note—Beginning of menstruation with 16 years, married at the age of 17. A few years later gave birth to a baby boy. The patient bled again after a year and since then she is constantly bleeding. She was treated with Progynon, Proluton and testosterone propionate. After 6 months of continued bleeding she came to our out-patients department. She complained of evening rise of temperature upto 99°F, loss in weight upto 3 seers within last 3 months, no appetite, constipation and backache. Examination showed a thin lean person with very pale looks, lungs healthy and no tenderness in lower abdomen. P. V. examination revealed a retroverted normal-sized uterus, nothing abnormal in adnexæ. Vaginal smear contained red blood cells, white blood cells, staphylococci, Döderlein's bacillus; tubercle bacilli were negative. Blood count: Hb—40 per cent, erythrocytes—2 million, leucocytes—7,000, per c.mm: lympho—31 per cent, large mono—3 per cent,, polymorphs.—66 per cent. Yoshida's test strongly positive.

Treatment

The treatment of such menstrual disturbances lies in the following—(*a*)looking after the general health, (*b*) removal of the salt disturbance and (c) endocrine therapy.

It is very important to look after the general health of a patient. Rich food should be given as far as possible. The patients should get plenty of milk, butter, fruits, etc., as much as they can possibly digest. There is always lack of appetite. There is often a great distaste for food. The appetite creating mixture usually fails. Vitamins help in bringing out the calcification of the tubercles and remove the disturbances of mineral salts. They are prescribed as vigantol or adexolin 3-5 drops thrice daily; the poor patients get one dram of cod liver oil in emulsion or with fruit juices thrice daily.

There is a great difference of opinion on the administration of calcium. Hypocalcæmia is not known to accompany tuberculosis and calcium administration even for a long time does by no means raise the blood calcium beyond usual limits. The best form of calcium therapy is to augment the calcium content of the diet. This form of augmentation of calcium is sometimes not possible. In our opinion calcium should be administered preferably as calcium gluconate per intravenous injection. The patients begin to improve in health, increase in weight and have better appetite. Alexander has suggested afenil injection and Toneff Collosal Iodine preparation.

Schittenhelm, Kuczynski, Neufeld, Meyer, Watrum, Siegmund, Dietrich and Singer have tried to increase the functional activity of metabolic processes of the reticulo-endothelial system with different medicines but experiments have so far not been unsuccessful on human beings. Hydroxyl preparation of fibrin has been suggested in the Russian literature but it still requires trial.

These conditions are fulfilled by the administration of A. O. vaccine.

The tubercle bacillus is composed of albumen, protoplasm and a large quantity of waxy substance. The former two act as the immunity promoters and the latter counteracts and hence is useless and, therefore, it is taken away during preparation. Further, A. O. is a polyvalent vaccine and is devoid of allergic reaction.

Dr. Arima has suggested 50 units of A. O. vaccine per 50 Kilograms weight or more. He gives as a routine one injection every week. On the first day there is a little malaise and, therefore, the patient should take complete rest. In weakly positive cases 10 c.cm. were given, in moderately positive 14 c.cm. and in strongly positive 20 c.cm. in all.

A day after the injection the patients have a refreshed feeling. The appetite begins to increase. The fever decreases in course of time. Dysmenorrhœa improves. The flow of the blood gets better. Interval comes to normal in all the cases excepting two. On account of the prolonged treatment we lost their sight. The irregular bleedings are changed to normal menstruation as described in the case reported.

The substitution therapy of endocrine is absolutely useless as long as the disease is not cured. The menstruation may appear once or twice but then again fails to come. So this expensive therapy becomes useless. After the patient has improved in health and the menses still do not appear, then only the endocrine therapy should be resorted to.

I advocate ½ mg Stilbœstrol thrice daily instead of Progynon, etc. The menstruation becomes regular in course of time. In order to keep away the effect of tubercular infection, courses of A. O. vaccine should be given every year.*

REFERENCES

HELDT (1937)—*Gynec. et. Obst.*, 35:327.
HUNT (1934)—*Am. J. Obst. & Gynæc.*, 28:277.
KAPUR and KAUL (1939)—*J. I. M. A.*, 6:352.
KAPUR and SAROJINI (1940)—*J. Obst. & Gynæc. Soc. of Northern India*, 1:119.
LIEGNER (1935)—*Zeutralbl f. Gynäk*, 2833.
MAYER (1933)—*Rev. franc. de gynéc. et. d'obst.*, 28:323.
YOSHIDA (1936)—*Kekkaku*, 9:69.

*Read at the Scientific Section of the XVII All-India Medical Conference, Vizagapatam, Dec., 1940.

THE AMBIVALENCE OF SEX HORMONES IN THERAPEUTICS

A. P. PILLAY, O.B.E., M.B.B.S.,
Bombay

The hormones discussed in this paper are the male hormone, the follicular hormone and the luteal hormone.

There is still unfortunately a belief even among members of our profession that the male sex hormone when administered to females has nothing but a masculinizing effect and *vice versa*. This is true only when massive doses of the hormones are used and that for a prolonged period. As regards the male hormone, Salmon, Geist and Walter (1940) are of opinion that in women only doses over 500 mg. in one menstrual cycle give rise to signs of masculinization, such as hoarseness of voice, facial hirsuties, suppression of menstruation and so on. There are no authenticated cases of feminization of the male by the administration of the female hormones, though it is recorded that in the pioneer stages of the synthetization of follicular hormone it was noticed that absorption of the hormone through the skin of the hand caused the facial hair to fall off in the male workers. In this connection we have to remember that massive doses of male hormone in the male and female hormones in the female also cause depressional and other adverse effects.

It is recognised now that the two sexes have hormones of the opposite sex in their circulation and excretions. This means that in treating males and females with hormones of the opposite sex, we are introducing nothing that is not already present in the system.

The author (1940) discussed in detail his conclusions as regards the therapeutic value of the hormones of one sex in the other. Here only a few hints are given so that the ambivalence of sex hormones may be made use of in treating sex and genital disorders of both sexes. I personally find that the hormone of the opposite sex alone or with that of the same sex has often a greater therapeutic value in some types of cases than the hormone of the same sex when used alone.

THERAPEUTIC USES OF THE MALE HORMONE IN FEMALE SEX AND GENITAL DISORDERS

This subject has been studied in more detail by many workers than the subject of the uses of the female hormones in male disorders, which has not been subjected to much clinical trial by others as I have done though in a comparatively limited number of cases.

The admitted uses of the male hormone are:

(1) In dysmenorrhœa, it relieves the pain and discomfort.

(2) In menorrhagia and metrorrhagia, it stops and even regularises the bleeding.

(3) In threatened abortion, it stops the bleeding and contractions of the uterus and allows the pregnancy to continue.

(4) In menopause, it relieves the nervous, vascular and articular symptoms.

(5) In mastitis and pain in the breasts caused by premenstrual congestion or other causes, it gives immediate relief.

(6) The male hormone suppresses ovulation and delays menstruation temporarily when it is found to be necessary to do so.

The action of the male hormone in most cases in the female, especially in menopause, is believed to be through its inhibiting action on the gonadotropic hormone of the anterior pituitary glands. Then again, the physiological action of testosterone and progesterone is similar in many ways and the one reinforces the effect of the other. A combination of the two hormones relieves the symptoms more rapidly in cases like threatened abortion, etc.

THE THERAPEUTIC USES OF FEMALE HORMONES IN MALE SEX AND GENITAL DISORDERS

(A) *The Follicular Hormones.*

(1) In infantilism, it reinforces the effects of the male hormone and accelerates the growth of the accessory sex organs.

(2) In defective erection, it brings on erections by increasing the vascularity of the sex organs.

(3) In defective libido, increased desire for copulation is brought on by its reflex vascular action on the genital system.

(4) In delayed or absence of ejaculation it causes ready ejaculations by increasing the secretions of the accessory sex organs and the paristalsis of the passage through which the semen passes.

(5) In oligospermia and asthenospermia it increases the quantity of semen and increases the motile power of the spermatozoa.

(6) In oligozoospermia, when used with the male hormone, it activates spermatogenesis.

(7) By the reinforcing action of the female hormones on the male hormone only smaller quantities of the latter are required to bring on the required therapeutic results.

(B) *The Luteal Hormone.*

(1) In premature ejaculation, nocturnal emissions —prostatorrhœa and spermatorrhœa it brings on relief by decreasing the vascularity of the genital passages and accessory sex organs and by desensitizing them.

(2) In satyriasis and other cases of increased libido it depresses libido and erectile power by its direct desensitizing effect on the sex centre in the brain and also by reflex action through the devascularised sex organs.

(3) In sexual neurasthenia when used alone or with the male hormone, it relieves the symptoms.

(4) The male hormone when used with the luteal hormone is believed to prolong the therapeutic action of the latter. (Foss, 1939).

To achieve these results, effective preparations should be used. Excellent synthetic preparations of all the sex hormones are now available. "Of all the synthetic male hormones, testosterone alone acts like the natural hormone." (Steinach and Kun, 1940).

As regards the female hormones, œstradiol depropionate and progesterone give the best results.*

REFERENCES

Foss (1939)—*Lancet*, 1: 502.
FRANK (1940)—*J. A. M. A.*, 114: 1504.
PILLAY (1940)—*Indian M. Gaz.*, 75: 404.
SALMON, GEIST and WALTER (1940)—*Am. J. Obst. & Gynec.*, 38:
STEINACH and KUN (1940)—*Lancet*, 1: 688.

* Read at the Scientific Section of the XVII All-India Medical Conference, Vizagapatam, Dec. 1940.

NOTICE

The attention of the members of the Association is respectfully drawn to the notice on advertisement page v of this issue of the journal regarding the procedure to be adopted in case of non-receipt by them of any issue of the journal.

A. K. SEN,
Secretary, J. I. M. A.

JOURNAL OF THE

INDIAN MEDICAL ASSOCIATION

CALCUTTA, JULY 1941

ACTION OF SEX HORMONES ON THE HEART, LIVER AND KIDNEYS

Some of the properties of hormones of female sex organs were found out long before the endocrine functions of male sex organs were specially studied. Empirical use of testicular products were, however, known from prehistoric ages of Ayurveda and in the present age Voronoff's researches on monkey glands culminated in the grafting of testicle, pituitary and other internal glands for so-called rejuvenation. Steinach's procedure of sterilisation by cutting out portions of vas deferens was followed by observations on its reaction on the prostate gland and on general improvement of bodily functions akin to rejuvenation. An important discovery was made when it was found that gonadotropic hormones secreted by the anterior lobe of the pituitary gland controlled the production of œstrin by the ovary. It was subsequently found that there are mainly two different kinds of anterior pituitary hormone, one of which, prolan A, causes the ovarian follicles to ripen, and after the rupture and release of ovum, another pituitary hormone, prolan B, effects lutinisation of the ruptured follicle forming the corpus luteum. Careful study was made of the action of œstrone secreted by the ovary during its ripening period on the proliferation of the mucous membranes of the uterus during the first half of the intermenstrual periods. Similarly, the action of the hormone of corpus luteum on the second or progestational phase was carefully studied. The therapeutic indications of œstrone and of œstradiol esters in amenorrhœa, dysmenorrhœa, menorrhagia, sterility, various menopausal disturbances and associated conditions like pruritus vulvæ, arthritis, climacteric hypertension and such others were put to trial and the results reported to be satisfactory.

So also the hormones of corpus luteum (progesterone) were found to be effective in threatened or habitual abortion, vomiting of pregnancy and in certain menstrual disorders. A synthetic preparation of natural œstrogen, stilbœstrol, first described by Dodds and others (1938), was put to extensive clinical investigation under the auspices of the Medical Research Council, London. It was found that 1 mg. of stilbœstrol by mouth was equivalent to 500 international benzoate units of œstradiol benzoate. Again, placenta was found to contain three biologically active substances, *viz.*, (1) œstrin-like (2) anterior pituitary-like principles and (3) emmenin; and placental extract is used in dysmenorrhœa, amenorrhœa and for passive immunisation in measles.

In the case of male sex organs, the study of their endocrine functions took a long time to materialise tangible results. The isolation of active principle from male sex organs and from urine was only recently effected. Esterification of these hormones as acetate, propionate and such others increased their activity enormously on the sex organs. The therapeutic indications were chiefly confined to maldevelopment of the sexual organs and disorders of male sexual functions. Subsequently, endocrine affection of the accessory genital organs came to be treated, the most important of which are prostatic hypertrophy in men and mastopathy in women. Besides, it came to be exhibited in disturbances of the masculine critical age, senility and certain neuroses associated with disturbances of sexual functions.

Another important fact came to be recognised that every man and woman is of the nature of a hermophrodite as each possesses certain organs of the opposite sex, inspite of the predominance of his or her own special organs. In 1934, œstrogens were isolated from male urine and in 1936, androsterone and transdehydro-androsterone were found to be naturally present in the female organism by Callow. In 1940, œstrone and œstradiol were recovered from testis by Beal. It was already found that the follicle stimulating factor of the anterior pituitary is gametogenic in function, that is to say, it stimulates the male germ cells, the ova and the granulosa. The lutinising factor appears to act predominately on the cells of the ovaries as well as on the

Dodds and others (1938)—*Nature*, 141 : 241.
Callow (1936)—*Chem. Industr.*, 55 : 1030.
Beal (1940)—*Biochem. J.*, 34 : 1293.

interstitial cells of the testis. It has been experimentally ascertained that with the decline of the genital life in advanced age, there is a relative preponderance of secretion of female hormone fraction over the male hormone normally secreted by the testis and that the gonadotropic hormone of the anterior pituitary body is increased leading to an increase in the size of the prostate. It has been assumed by many authorities that Sertoli-cells of the testis secrete a special hormone inhibiting the pituitary activity, explaining the indications of endocrine treatment of prostatic hypertrophy.

Recently, researches were instituted in the Lister Institute, London, under the grants of the Medical Council on the effect of sex hormones on *non-sexual* organs like the liver, heart and kidneys by Korenchevsky and his associates (1941). They found that large doses of œstrogen produced depressing effect on the growth and body weight as well as on fat deposition in the body and that large doses of œstrogen exert toxic action on the liver, by decreasing its weight. Moderate doses have been found to have a stimulant effect on the liver and kidneys in both males and females. The ester of testosterone (propionate), causes a decrease in body weight, similar to large doses of œstrogen, but it has a strong stimulant action on the heart and liver, as manifested by increase in weight of these organs.

It appears, therefore, that hormones of both male and female sexual organs exert strong stimulating action on the heart, liver and kidneys, and combination of both hormones shows better results if judicially employed. It has been seen that best effects are obtained when small doses of œstradiol esters (benzoate, butyrate) were administered at long intervals between daily injections of male hormones. We await confirmation and further development of these important findings.

Korenchevsky and associates (1941)—*Brit. M. J.*, 1: 396.

WANTED A LIBRARY

We are feeling every day the necessity of a good reference library. The Journal of the Indian Medical Association is suffering from this want all along. It is high time that steps should be taken by all concerned to remove this long felt and everyday growing want.

The Editor, Journal of the Indian Medical Association, will gratefully accept any book, journal or medical publication, recent or old, which members may kindly present. Such gifts will be duly acknowledged in the columns of the Journal. Gifts of monographs and books written by members will be specially appreciated.

NILRATAN SIRCAR,
Editor, J. I. M. A.

CASE NOTE

FOREIGN BODY IN THE LUNG

MANINDRANATH GHOSH, M.B.
Calcutta.

A boy of 8 months was seen for the following complaints:

(*a*) Diarrhœa for a week—7-8 liquid yellow stools a day. (*b*) Continued pyrexia for 3 days. (*c*) Cough.

Physical Findings

Tongue coated and moist, abdomen a bit tumid, liver a little enlarged but moderately hard, spleen just palpable, general condition fair. Nothing detected in other systems.

Course and Treatment

The diarrhœa was controlled in 3 or 4 days but the temperature was continuous for about ten days with a peak of 103°F and coming down to 100°F. Then there was a remission for a whole 24 hours. It shot up again and rose up to 105°4 even for 2 or 3 days and came down to normal then. With quinine the maximum level was lowered but it did not stop.

The cough persisted but during these days nothing incriminating could be detected. By the 14th day the air entry in the left lung upper lobe was impaired. A very faint breath sound of the nature of tubular breathing (?) could be heard on a very careful auscultation. But the area was stony dull; V.R. and V.F. were impaired markedly. The apex beat was not displaced. The temperature was running in a whim, as it were. Some days it was intermittent; it was continuous for 2 or 3 days with a break to rise again for a day or more.

At this stage, a consultant was called and he diagnosed it to be a case of empyema. A skiagram was taken and the opinion was—a delayed resolution of pneumonia. The baby was given glucose, quinine, calcium, M & B 693, alkalies, stimulants etc. But, clinically there was no improvement. The general condition was marching down hill. One could, in no way reconcile oneself to the diagnosis. When matters were drifting in this way, one morning there was a terrific fit of coughing and the boy was on the verge of suffocation and the family members were in despair of his life, when he expectorated a cheesy mass having a nucleus of a decomposed whole pea. This set all our attempts at rest and the child was saved. From the very day, the temperature ceased to rise. General health also was regained gradually.

Discussion

When the foreign body tries to pass through the larynx the latter is thrown into a spasm and it is coughed out. When it remains in a laryngeal ventricle it may cause partial or complete loss of voice. If it at all manages to pass the sentinel, the tracheal mucous membrane also excites cough at the outset. But peculiarly, later on, there is a variable period of absence of symptoms, when it gradually goes down the trachea and the bronchus. An interval has been recorded of 26 years between the initial accident and the removal of it. At last it lodges somewhere in the bronchial tree. It sets up irritation and cough restarts. There mild inflammation ensues with profuse mucoid expectoration. Thus the passage is partially or completely blocked and it causes partial or complete collapse of the lung. The air being absorbed the area becomes dull on percussion. Gradually the lung parenchyma may be involved in it and an abscess may be formed. Bronchiectasis, empyema, pleurisy and fibrosis of the lung are not rare. If the foreign body be sharp it might cause hæmoptysis and it may pass through the lung and set up pleurisy or empyema. Due to anatomical reasons the right lung is more vulnerable as it is wider and more vertical. But queerly, the case in point is an exception.

Nandi (1931) recorded three cases, two of which also were left sided. There, the incriminating article was *supari* (nut) in two—one victim was a doctor and *chana chur* (fried *dal*, gram, etc.) in one. Children, sleeping with betel nut etc. in their mouth stand such risk.

In a later phase the symptoms very much resemble tuberculosis of lung. There are irregular pyrexia, chill, sweating, irritation and profuse purulent and mucopurulent expectoration which sometimes may be offensive. But repeated sputum examination is negative to acid-fast bacilli.

Two points are to be noted: One is that no notable symptom may occur when the accident occurs, as the article may pass very rapidly. The second point is that there may be a period of quiescence between the accident and development of symptoms of inflammation.

This accident is not so uncommon. Children are the usual victims. Needles, pins, toys, fragments of bones and various organic materials *viz.*, pieces of meat, seeds, peas etc. are the common offending articles.

Reference

Nandi, P. (1931)—Massive collapse of the Lungs. *Calcutta M. J.*, 26: 51.

CURRENT MEDICAL LITERATURE

MEDICINE

Renal Insufficiency Following Transfusion

Daniel and Others (*J.A.M.A.*, 1941:16:1208) write that of 13 patients with renal insufficiency following transfusion 6 recovered and 7 died; an immediate or delayed reaction occurred as a result of the transfusion and was followed by nausea, vomiting, hæmoglobinuria, jaundice, oliguria, stupor and uræmia. Of 6 cases in which blood grouping and cross matching were rechecked the blood in 4 was shown to be definitely incompatible and of the remaining 2, in 1 warmed, hæmolysed, stored blood 8 days old was given. Isohæmolysis unaccompanied by isoagglutination was found in 2 cases—this accounts for the error in cross matching and caused hæmolytic reaction. The pathological changes in the kidneys in 4 fatal cases consist of interstitial œdema, leukocytic infiltration, degeneration and necrosis of tubular epithelium and the deposition in the renal tubules of granular pigment derived from hæmoglobin. One case showed central focal necrosis of the liver cells.

The authors stress on the more careful cross matching of the blood of donor and recipient by the use of tube preparations incubated at 37·5°C for one hour which will prevent some of the errors and save lives. Citrated plasma should probably replace whole blood transfusion in the treatment of secondary shock and hæmorrhage. Alkalies should be administered to all patients prior to transfusion.

Acute Pulmonary Oedema

Luisade (*Medicine*, 1940:19:475) in a review on the subject points out that pulmonary œdema cannot be produced experimentally by overloading the left ventricle or induced by any mechanical procedure which is expected to produce pulmonary congestion. He suggests that the primary factor is neurogenic and it is only when this is present that simple mechanical changes in the cardiovascular system can produce pulmonary œdema. The nature of this neurogenic factor is obscure. Reflex stimuli arising in the heart and large vessels and in hollow viscera may be precipitating factors. Regarding pulmonary œdema caused by irritating gases the author writes that though these gases may cause such trouble by directly damaging the capillaries there are additional factors, nervous in origin, which are of importance.

Prophylactic Use of Sulphanilamide in Patients Susceptible to Rheumatic Fever

France and Reichsman (*J.A.M.A.*, 1941:116:551) report that during the last four years major rheumatic incidents were not observed in groups of known rheumatic subjects who had been placed on daily prophylactic dose of sulphanilamide during the fall, winter and spring months. The toxic effects regulating from this prolonged dosage with sulphanilamide were negligible. This report thus presents a hopeful picture for the use of the drug in the prophylaxis of rheumatic fever and certainly shows that the drug may be used in small daily doses for long periods with comparative safety.

Theophylline Mono-Ethanolamine—Its Use In Asthma and Other Allergies.

Lamson and Bacon (*J.A.M.A.*, 1941:116:915) from observations on 153 patients with paroxysmal dyspnœa refractory to conventional therapy treated with theophylline mono-ethanolamine (Thiemin-Lily) report that approximately 10 per cent obtained no relief, that the drug is useful in small doses by mouth and in small amounts intravenously, that there is a slow development of tolerance even to the small quantities, that untoward reactions were inconspicuous and tended to be limited to the first few days (nervousness and gastrointestinal symptoms and these were kept at minimum when the drug is taken with some food). 0·2 gm. every 6 hours with total 0·8 gm. will give relief without any side effects. The authors maintain that the drug will be a valuable adjunct if not a substitute for ephedrine in the treatment of asthma.

The Effectiveness of the Xanthine Drugs In Treatment of Angina Pectoris: Aminophylline

LeRoy (*J.A.M.A.*, 116:921) from the observations on 68 patients with angina pectoris treated with aminophylline or placebos in varying amounts report that in general aminophylline benefited 75 per cent of the sufferers, that placebos and sedative drugs only 20 per cent of the group, that when the patients who had been benefited by aminophylline were given placebos or stopped taking the drug about 80 per cent experienced a return of symptoms within less than 3 months. The dose of aminophylline used was 0·2 gm. three times daily.

Pain In Cancer

Lee (*J.A.M.A.*, 1941:116:216) writes that narcotics are not desirable in terminal cases of cancer and it is advisable to try non-narcotic medication before condemning the patient to a life of dependence on narcotic drugs. When narcotics are employed they should be regarded as analgesics and not as hypnotics. The minimal effective analgesic dose of a narcotic may be supplemented by hypnotic doses of a barbiturate in cases where hypnosis is considered desirable. The use of narcotics is apt to develop addiction and this should be avoided as in such case there is diminishing returns in analgesia and increasing discomfort due entirely to addiction itself. The best ways to control pain are care in nursing, x-rays and surgical measures and these are better managed in hospitals.

The Management of A Case of High Blood Pressure

Jones (*Practitioner*, 1941:146:72) writes that in the management of any given case the mode of life must be so regulated as to prevent mental and physical strain. Long hours of work must be avoided and patients whose occupation carries more than the average amount of anxiety and worry should be ordered to take a period of rest or relaxation for half an hour to an hour after the mid day meal, before beginning the work of the afternoon. Adequate holidays also have a very important place in the treatment of hypertension and, when the rise in blood pressure is persistent and resistant to other methods, a long rest from work may be required. Alcohol and tobacco both tend to raise the blood pressure, especially if indulged in to excess and they should be restricted. Meat and specially

red meat, should be given up entirely in severe cases and considerably reduced in all but the mildest types and meat soups which contain extractives must be cut out completely. In severe cases the diet should be salt-free as far as possible and in others the table salt must be eliminated. In obesity the total quantity of calories must be reduced. The adoption of fasting one day a week is another useful regime. The use of drugs should be considered under three main groups, sedatives, vasodilators and diuretics. Sedatives are indicated specially in cases where nerve strain and anxiety are predominant features. Luminal in doses of ½ grain two to four times a day or combined with theobromine as theominal in 5 grain doses once or twice a day is very effective. Cases not responding to luminal will respond to bromide and phenazonum in grain 10 doses and in cases where insomnia is a distressing complication hypnotics such as dial and medinal may be used with benefit. Vasodilator drugs include drugs causing either a temporary fall in blood pressure such as amylnitrite, nitroglycerin, etc., or permanent fall such as nitrites and nitrates, xanthine and choline decrivates. Diuretics specially of the mercurial variety are particularly useful in cases of hypertension associated with left-sided failure, *viz.*, cardiac asthma or pulmonary œdema. Spa treatment has its place in the treatment of this condition specially in cases who are unwilling to submit to dietitic restrictions and take physical exercises. Diathermy is also useful for patients who do not improve readily when treated by conventional therapy. For hypertension itself long wave diathermy is of most value. In angina of effort ultra-short-wave diathermy through the chest, front and back often improves the exercise tolerence of the patients and may eventually cause its disappearance.

SURGERY

Treatment of Renal Tuberculosis

Herbst (*Bull. New York Acad. Med.*, 1941:17:61) writes that the general medical-surgical consideration of the treatment of renal tuberculosis calls for a comprehensive understanding of many factors which are involved in each case. These factors are: (1) extent of renal process—(a) miliary, (b) necrotic destructive and (c) nephritic; (2) extent of extra-renal lesions—(a) bilateral involvement, (b) bladder involvement, (c) genital involvement, (d) pulmonary and (e) other extraurinary lesions; (3) factors affecting general resistance—(a) economic, (b) psychogenic, (c) climatic—ultra-violet ray, (d) pain, (e) co-existing bacteriuria, (f) food and (g) medication, tonics.

The acute miliary lesion should not be treated surgically because it is bilateral and usually a terminal fatal process. The tuberculous nephritic patients should be treated medically and all measures to conserve and build up general resistance instituted. The destructive parenchymatous lesions involving any more tissue than one minor calyx should be subjected to nephrectomy unless there are serious contraindications to surgery from a risk stand point. Bilateral destructive lesions usually call for medical treatment but in cases in which one side is extensively involved and the other side has minimum involvement nephrectomy of the 'bad kidney' is indicated. When bladder symptoms are severe and progressive nephrectomy is indicated. Persisting bladder symptoms call for the following treatment, in order of relative risk: urinary antiseptics for mixed infections; Caprokol when tolerated and effectual; increasing strength of phenol lavage, when effective, upto 6 per cent; intrathecal alcohol injection; presacral neurectomy. ureterostomy, ureterosigmoidostomy.

In genital involvement medical measures should be adopted until the lesions become destructive when suitable surgery will be necessary. Pulmonary and other extraurinary lesions should be combated according to the accepted tenets.

Primary Carcinoma of the Lung

Ochsner and DeBakey, (*New Orleans M. & S. J.*, 1941: 93:387) write that the incidence of primary carcinoma of the lung is definitely and steadily increasing, that the lung ranks second only to the stomach as the primary site of cancer and that it occurs predominantly in the male sex and its most frequent incidence is in the fifth and sixth decades. There is no characteristic clinical picture of early carcinoma of the lung and the condition should be suspected in every patient past forty years of age who complains of cough that cannot be reasonably explained and that does not readily respond to appropriate treatment. Metastases occur by direct extension through the lymphatics, by way of blood stream and by 'bronchial embolism'. The most frequent sites of metastatic involvement are regional lymph nodes, next most frequent is the liver. Amongst the available methods of diagnosis rœntgenography, bronchoscopy and bronchography are of great value and will provide an accurate diagnosis in majority of cases (over 70 per cent). Radiation therapy is of little or no value in the treatment of the condition and the only curative treatment is surgical extirpation of the involved lung. The results of such treatment are as follows: in the collected cases (110 cases) the mortality rate was approximately 60 per cent and in the personal series (19 cases) 47·3 per cent. The operation is done in the following way: In general two approaches may be made, either an anterior or a posteriolateral. After entering the pleural cavity and freeing all adhesions, the hilar structures are exposed by incising and mobilizing the mediastinal pleura. The hilar vessels are isolated individually and divided between transfixation-ligation sutures of silk. The bronchus is severed between clamps and the stump closed by matress sutures of silk. The mediastinal nodes are carefully extirpated. It is for this reason that individual isolation of the hilar structures should be done. Mass ligation does not permit removal of these glands. Pleuralization of the stump of the hilar structures is performed by approximating the anterior and posterior mediastinal flaps. The pleural cavity is closed without drainage.

Early Diagnosis of Malignant Metastasis to the Spine

Wolfson and others (*J.A.M.A.*, 1941:116:1044) write that adequate roentgen therapy of malignant metastatic lesion often produce such dramatic relief of pain and such remarkable regression of the lesions that an early diagnois of such condition is imperative. The authors give the following triad for an early diagnosis of spinal metastasis: (1) the presence of radicular pain, in narrow zones, sharply limited to one or two special nerve roots associated with localized tenderness to deep per-

cussions on the spinous processes of the vertebrae which form the foramen for exit of the nerve roots of the painful dermatomes; (2) an accelerated erythrocytic sedimentation rate and (3) an increase in the serum phosphatase level. This diagnosis is made irrespective of negative roentgenologic findings.

The use of Sulphanilamide in Peritonitis

Michel (*New Orleans M. & S. J.*, 1941:93:419) reports on the use of sulphanilamide in large doses in 14 patients with peritonitis of various types with no mortality. The number of cases reported are too small to draw any definite conclusions but the results justify the further trial of this therapy. The use of sulphanilamide in peritonitis is based on 3 principles: (1) The presence of sulphanilamide in large concentrations in the fluids and exudates of the peritoneal cavity; (2) the specificity of sulphanilamide in combating the micro-organism most frequently isolated in peritonitis; (3) the property of the drug to be more effective against lesions presenting the pathologic characteristic of rapid spread with little local reactions and necrosis such as is present in peritonitis. A normal saline solution containing 120 grains of crystalline sulphanilamide to each 1,000 c.c. is administered as a hypodermoclysis—the average adult dose is 250 c.c. every 6 hours and is given on the lateral aspect of the thighs, with no serious discomfort to the patient. The dose is either continued for several days or gradually reduced depending on the response of the patient. The blood concentration should be kept above 5 mg. until the infection is under control. No local necrosis occurred in the series nor any serious toxic reactions; however, the toxic effects are not to be underestimated and should be carefully guarded against. The advantages of giving sulphanilamide by hypodermoclysis in cases of peritonitis over oral administration are: (1) surety and rapidity in absorption and (2) avoidance of such troublesome complications as nausea, vomiting and distension.

Osteomyelitis And Pyogenic Infections of Joints

Cleveland (*Bull. New York Acad. Med.*, 1941:17:205) writes that hæmatogenous acute osteomyelitis and arthritis is a disease of childhood and adolescence with males more frequently involved than females. The bacteria responsible have been staphylococcus in nearly 80 per cent and streptococcus in most of the remainder and there seems to be a selective action on the part of these two bacteria, staphylococcus in the main affecting the bone primarily and if a joint is invaded it is by extension; streptococcus tends to invade the joints primarily and predominates in infants. The bones and joints of the lower extremity and other weight bearing bones and joints are much more frequently invaded than those of the upper extremity and of the long bones, the femur was most frequently invaded in the series. Approximately 30 per cent of these patients had more than one focus of infection. Complications met with were ankylosis of joints, fracture and growth disturbance. Mortality was 8·8 per cent of the 34 patients seen in the acute stage of their disease. Treatment in the acute stage is supportive: infusions, transfusion, morphine and protection of the involved extremity. When there are definite signs of suppuration rapid drainage through small carefully placed incisions with least trauma followed by immobilzation with circular plaster of Paris splints offers the best treatment.

Intubation Management of Distension In Intestinal Obstruction

Bennet (*West. J. Surg.*, 1941:49:71) writes that though intubation by no means replaces the surgical management of intestinal obstruction the judicious use of this procedure will materially reduce the mortality and morbidity of non-strangulating type of obstruction. When correctly indicated and properly used it constitutes an aseptic enterostomy and for practical purposes it replaces the external decompression operation with the exception of cæcostomy. The author stress on the following points:

1. Levin-tube suction should be avoided when there are suggestions or very early manifestations of organic obstruction of small bowels as in the latter case it is inadequate. 2. Intubation decompression should be attempted only after the intra-abdominal conditions which locally jeopardize the vascular integrity of segments of bowels have been considered and excluded. 3. Intubation decompression is the procedure of choice in treating paralytic ileus:—the process is slower but results are uniformly good. 4. The use of Miller-Abott tube is indicated in preoperative and postoperative management of obstructive lesions of the colon. 5. Intubations management may be successfully accomplished after the surgical performance of alterations of the normal continuity of the gastrointestinal tract.

OBSTETRICS AND GYNAECOLOGY

Management Of Lactation And Of Disorders Of The Breast In The Puerperium

Kenny (*Practitioner*, 1941:146:18) points out the steady decline in breast feeding in the country and mentions amongst others the following as responsible factors, *viz.*, the indifference on the part of the average practitioner to the importance of breast feeding and the ready supply of cheap artificial feeding substances from subsidized infant welfare clinics.

Management of lactation. The expectant mothers are given instructions relating to care of the breasts, stressing the need to wear a well-fitting bust bodice to support the growing breasts and keep the nipples clean with soap and water and to draw out the nipples if they are depressed. After delivery the baby is put to breast at regular hours and the nipples are swabbed clean with boracic lotion both before and after each feed and kept dry to prevent the formation of cracks in them; when cracks develop they should without delay be treated by painting with tincture benzoin co. and a glass nipple shield worn till they heal. The mother should get a pint and a half of milk daily, extra fluids and a balanced diet of the caloric value of 2,800. If these routine measures fail lactogenic hormone of the anterior pituitary (prolactin) should be injected in the early stage of lactation. The total dosage employed is 15 c.cm. (900 Riddle units) in each case spread over five days thus: First and Second days 5 c.cm. daily (2×300 R.U.), third and fourth days 2 c.c. daily (2×120 R.U.) and fifth day 1 c.cm. (60 R.U.)—this is given

by intramuscular injection into buttock or arm and should produce no ill-effect.

Disorders of the breast in the puerperium. These are either traumatic (cracked nipples) or infective. Treatment of mastitis should be promptly carried out. Prophylaxis consists of taking proper cares of the breast and treatment of the cracked nipple. With the appearance of the symptoms of mammary infection the breast should be put at rest by closely bandaging the whole organ in the most comfortable position and applying an icebag or hot fomentation; the child should not be allowed to suckle and the flow of milk should be suppressed by using stillbœstrol 2 mgm. daily for 3 days. M. & B. 693 (3 gm. daily) may be given with advantage—this therapy is usually effective if begun with early stage of the infection. When the inflammatory process is not checked and there is formation of definite pus the breast is incised with the first appearance of fluctuation under efficient general anæsthetic and drained. Repeated aspirations done through a wide bore needle followed by irrigation with normal saline through the same needle will in some cases suffice to drain the abscess satisfctorily and should be done in cases who are unwilling for cosmetic reasons to have open operation.

Treatment of Chronic Cervicitis

Black (*Arch. Phys. Therapy. Ref. Gen. Practitioner*, 1941:11:291) summarises in the following lines the treatment of chronic cervicitis:

1. A pelvic examination is incomplete without inspection of the cervix by one who is familiar with the gross pathologic processes of the cervix.

2. Every erosion of the cervix should be regarded as a potential carcinoma. Biopsies should be made in all suspicious cases.

3. Superiority of electrosurgery has been recognized to an extent as to have relegated plastic surgery to the background, yet the latter still has a definite place in selected cases. Extensive lacerations in chronic cervicitis are best treated by operation. For lacerations less than 1½ cm. in length cauterisation is most suitable; the result is equally good and there is less danger of malignancy following this procedure.

4. Amputation of the cervix should not be performed during the child-bearing age, but in the elederly an amputation is indicated in the presence of a badly disceased cervix with multiple lacerations. Sturmodorf's or a modified Schröder operation, is preferable for young women with an elongated hypertrophied cervix.

5. In chronic cervicitis limited to the endocervix, small cautery points should be used. Chronic interstitial cervicitis with moderate hypertrophy and only a few cysts should be treated by deep lineal burns and puncture of the remaining cysts with a cautery point.

6. For a large, cystic, degenerated cervix with extensive hyperplasia, ionization is preferable. Cysts not removed by this method may be punctured with a cautery point. If a laceration of moderate degree is present, this should be cauterized.

7. Postoperative care is most important following electrosurgery to prevent atresia or stenosis.

8. Electrosurgery should not be undertaken during an acute infectious process. If the uterus is retroverted, and especially if the cervical canal is patent, the danger of complications is increased. Unless imperatively indicated, the uterus should not be invaded at operation, as dilatation and curettage of the uterus materially add to the possibility in infection.

9. Because of the variety of bacteria present in chronic cervicitis, the patient should not be led to believe that there is no danger in either electro-surgery or plastic surgery. A small percentage of patients may succumb from an infection; a larger number are gravely ill for weeks. Others are never completely cured of residual disease following acute pelvic infection.

10. The cervix has remarkable recuperative powers, and if good surgical judgment is exercised in the selection of the tratment of chronic cervicitis, excellent results may be anticipated.

PEDIATRICS

Treatment of Congestive Failure in Children with Acute Rheumatic Fever

Walsh and Sprague (*J.A.M.A.*, 1941:116:560) in reporting on the effects of various drugs on the heart and circulation in 44 consecutive cases of heart failure during acute rheumatic fever observe that the xanthine diuretics were found to be of greatest value, in particular theobromine calcium-salicylate or theobromine sodium-acetate (in the dose of 1 gm. three times a day), that theobromine sodium-salicylate given by mouth was found less effective but was useful when given rectally, that mercurial diuretics given intravenously are effective in producing diuresis but should not be given immediately after full digitalization because of the danger of inducing toxic digitalis reaction during the loss of fluid, that digitalis is found to be of distinct value but it was found necessary to use great care in its administration.

Diuretics of the xauthine group are the first choice; if they fail digitaliss may be tried if one estimates doses according to weight and bears in mind that children with rheumatic fever and congestive failure are specially prone to intoxication with digitalis. The mercurial diuretics are reserved for those in whom heart failure is increasing inspite of the use of xanthine derivatives or digitalis.

The Care of the Premature Infant

Strong (*Tri-State M.J.*, 1941:13:2658) writes that any baby which at birth weighs less than 5½ pounds or measures less than 17½ inches may be considered as either immature or prematurely born, according to whether the estimated period of gestation is full time or less. If their lives are to be saved there are three fundamental requirements which have to be fulfilled. The first is the maintenance of the body temperature, the second one is adequate nutrition and the third one is the prevention of infection. Immediately after birth the infant should be wrapped up in a warm blanket. It is also important not to cut the cord until pulsation has almost disappeared—this requires from one to five minutes during which time the infant will receive from 30 to 60 c.c. of blood from the placenta

and it should not be deprived of this all important additional blood by tying off the cord too quickly. The cord should also be kept sufficiently long to allow for a second ligature as the first one may cut completely because of the frail make-up of the vessels. The care of the skin is of paramount importance in the premature and the slightest trauma may mean the difference between saving the baby or losing it. The infant should be kept at a constant temperature at a point between 80°F to 90°F and it should be remembered that overheating is sometimes as harmful as chilling. Provision should also be made for proper and adequate ventilation. Premature or immature babies are not only anatomically imperfect but their entire physiology is insufficient for extrauterine existence. Their respiration is impaired for several reasons: anatomically atelectatic areas are common in the lung and as such surface areas for absorption of oxygen are greatly reduced; physiologically the establishment of medullary hæmatopoiesis and the discontinuance of blood production in the extramedullary erythrogenic centres (liver, spleen, etc.,) is much delayed in the premature, consequently the facilities for blood formation to equalize the rapid reduction of erythrocytes which occurs in all new-born babies are not established as rapidly in premature as they are under normal conditions and 'anæmias of prematurity' develop; the consequent reduction in erythrocytes as well as the hæmoglobin decreases the facilities for transportation of an already reduced intake of oxygen to the tissues; obviously the administration of oxygen for sometime after birth of a premature is desirable.

The average premature does better if it is not fed for the first 12 hours. A uniform schedule to be followed in the average is as follows: First 12 hours after birth: no feeding neither milk nor water. Second 12 hours after birth: 13th hour—boiled water (2-6 c.c.), 16th hour—boiled water (2-6 c.c.), 18th hour—breast milk (2-6 c.c.); 20th hour—boiled water (2-10 c.c.); 22nd hour—breast milk (2-10 c.c.); 24th hour—boiled water (2-10 c.c.). Breast milk is the best food for the premature. If for any reason it is impossible to obtain breast milk Similac should be used. It should be reliquefied in proportion of one tablespoonful to 4 ounces of water. As no premature baby has sufficient sucking power to obtain milk from the mother's breast it should be fed with an ordinary medicine dropper protected at the tip with rubber tubing usually clipped from a catheter. The feeding should be slow and careful so that every drop is swallowed and the food should be warmed each time. This should be continued until the baby is strong enough to use a regular nursing bottle. In those babies who cannot swallow at all, gavage is necessary. It is specially important to provide vitamins (specially A, C & D) and minerals in sufficient quantities to this type of infants. Concentrated vitamins are available and may be of great use to them. The greatest handicap in the care of the new born in the house is the possibility of the upper respiratory infections brought to it by other members of the family. The dangers of cross infections and skin infections in the average hospital are just as great as upper respiratory infections in the house. The importance of prevention of infection from any source is obvious.

RESUSCITATION OF THE ASPHYXIATED NEW-BORN INFANT

Rus and Strong (*Am. J. Dis. Child.*, 1941:61:1) classify asphyxia in the newborn as: (1) Mild asphyxia—the infant resists movements of the head and limbs, mucus plugs and amniotic fluid fill the mouth and pharynx. (2) Moderate asphyxia—muscle tonus absent, there is no resistance to opening of the mouth, no reflex irritation is induced by aspiration or by stimulation of the glottis. (3) Severe asphyxia—the infant does not respond to attempts at resuscitation; he appears livid or pallid; there is absence of any respiratory movements, and only an occasional flicker of the cardiac impulse may be detected through the thoracic wall; the upper respiratory tract has become a collapsed tube.

The following is the detail of treatment adopted: After the cord is cut the baby is received by the pediatrician in a sterile towel, placed on a table, immediately wrapped in the warm cover and the skin is gently, rapidly rubbed for a few seconds. The fingers of the doctor's left hand are placed beneath the neck of the child and the head hyperextended. With the intratracheal catheter, the nostrils, mouth, pharynx and nasopharynx are immediately aspirated of the mucus, amniotic fluid, blood or meconium. These three stimuli (warmth, cutaneous friction and aspiration of the upper respiratory tract) are usually sufficient to institute respiration in those infants who are mildly asphyxiated. If respiration does start, plain oxygen by face mask is administered for several minutes until respirations are regular in volume and rate or until the baby cries. In case respiration does not start alpha-lobeline is at once injected through the umbilical vein and the intratracheal catheter is introduced into the trachea with the left index finger introduced into the pharynx as a guide, gentle aspiration is performed until the trachea and upper brochii are clear and by means of the pediatrician's own breath from 5 to 10 gentle inspirations and expirations made, while the thoracic wall is watched closely for the amount of expansion. Quite after the limp pharynx begins to tighten and show some muscle tone which is definite indication that respiration will start. If respiration has started as is usual in the moderately asphyxiated infant, oxygen is again administered by face mask until the respiration is normal in rate and volume or until the baby cries. In the case of more severely asphyxiated infant when respiration will not start the catheter is withdrawn, the head again hyperextended, the face mask of Easton and Johnson resuscitator adjusted over the face, the alternate pressure and suction mechanism is started, plain oxygen being used at first. Coramine in doses of 2 minims is administered subcutaneously at 10 minutes' interval until respiration is established; 2 minims of epinephrine is given subcutaneously if the beat of the heart flags. If this fails the baby is placed in a small Drinker respirator with an oxygen tent over head.

After care is very important. All moderately and severely asphyxiated infants are placed in an incubator or warmed crib under oxygen tent for at least 12 hours or longer if necessary. Any irregularity in the respiration must be watched for and noted. A dose of 2 minims of coramine every 2 hours for 4 to 6 doses; insufflation of carbon-dioxide and oxygen by face mask for 2 or 3 minutes are given for 12 hours at 2 hours' interval. Orders are left for immediate use of epinephrine, coramine or the pressure suction apparatus of the Easton and Johnson resuscitator if cessation of respiration should occur. Intratracheal catheter is used to aspirate mucus from the upper respiratory tract if necessary, but the trachea should not be entered unless respiration stops.

NOTES AND NEWS

PUNJAB MEDICAL COUNCIL.

Extracts from proceedings of a meeting of the Punjab Medical Council held on 26th April, 1941:

Dr. Vishwa Nath was elected unanimously a member of the Executive Committee of the Punjab Medical Council.

Considered the cases of the following registered medical practitioners on whom notices were served to appear before the Council:—

(a) (*i*) Dr. Amar Singh, L.S.M.F.

The Council after hearing Dr. Amar Singh who was present in person resolved that as the case against him as put forth by the complainant does not stand fully proved the practitioner concerned is declared not guilty of infamous conduct in a professional respect. At the same time during the hearing of the case irregularities on the part of Dr. Amar Singh came to the notice of the Council, for these he expressed regret and was warned to be careful in future.

(*ii*) Dr. Gian Chand Chawla, M.B., B.S.

Dr. Gian Chand Chawla having joined the Indian Medical Service (Emergency Commission) could not be present before the Council. The Council after going through his case found him not guilty of infamous conduct in a professional respect.

(*iii*) Dr. Wasu Ram Kishan Chand, L.C.P.S.

The Council after hearing the Advocate and questioning the doctor declared Dr. Wasu Ram Kishan Chand not guilty of infamous conduct in a professional respect. There were, however, certain irregularities brought to the notice of the Council during the investigation of the case for which Dr. Wasu Ram Kishan Chand expressed regret and he was warned to be careful in future.

(*b*) Resolved that in future the complainant in a case should also be informed about the hearing of the case by the Committee and the Council.

The Council approved the report of the Sub-Committee appointed to consider the questionnaire issued by the Punjab Government Committee on Homœopathic system of Medicine and resolved that the members of this Sub-Committee should lead evidence on behalf of the Punjab Medical Council before the Punjab Government Committee on Homœopathic system of Medicine if so desired by Government.

The Council approved the report of the Sub-Committee apointed to draft rules and instruments of instruction for the visitation of Examinations by Members of the Punjab Medical Council.

The Council considered the inspection reports of the various Medical Schools and resolved that the reports be forwarded to the Principals of the Schools concerned for remarks and placed before the next meeting of the Punjab Medical Council.

The Council appointed a Sub-Committee to consider the draft of the Dental Bill.

The recommendations of the Executive Committee held on the 9th of April, 1941, was approved and it was decided that in future when further information with regard to a complaint against a registered medical practitioner is required Presidents of local Medical Associations, if any, should also be consulted.

MADRAS MEDICAL COUNCIL

Extracts from proceedings of the General Business Meeting held on the 7th October, 1940:

Dr. V. Rama Kamath was duly declared elected as Vice-President.

Dr. (Mrs.) O. M. Monahan was declared duly nominated member to the Madras Nurses and Midwives Council.

Dr. S. Sanjeva Shenoy, L.M.P., of Tandarampatti—Alleged abuse of rights conferred by Dangerous Drugs Rules.

The Council constituted itself as a court under section 17 (2) of the Madras Medical Registration Act, 1914 (Act IV of 1914) and dealt with the above case:

Dr. R. K. Narasimhachari, L.M.P., of Paramagudi—Alleged advertisement by means of handbills—Violation of paragraph 6 of Warning Notice.

Read the office note on the subject, and the letter of Dr. R. K. Narasimhachari, L.M.P., of Paramagudi, dated the 5th October, 1940, pleading his inability to appear before the Council.

The Council directed the Registrar to inform the medical practitioner—"That he is severely warned for not attending the meeting of the Council on the 7th October, 1940, when summoned to do so; and—That he is required to appear before the Council at its next meeting and answer the charge in person."

Read the letter from the Registrar, Bombay Medical Council, No. G|42-250 of 1940, dated the 11th May, 1940, to the Registrar, Madras Medical Council, regarding the advertisement of the Madras Chemical Industry, Limited, Madras, appearing in the *"Bombay Samachar"*, dated the 16th April, 1940, and other connected papers.

The following resolution was carried:—

"The Council directs the Registrar, Madras Medical Council, to inform the Registrar, Bombay Medical Council, that the Madras Medical Council is of opinion that the association of the names of registered medical practitioners with a chemical industry or any industry or trade can not itself constitute a breach of the Code of Medical Ethics unless infamous conduct in a professional respect is proved;

In regard to the particular advertisement of the Madras Chemical Industry, Limited, in the *'Bombay Samachar'* the Council learns after enquiry that the Madras Chemical Industry published the said advertisement without the knowledge and consent of the practitioners concerned who have since notified their protest and displeasure to the said firm."

Code of Medical Ethics—Paragraph 6 of Warning Notice—Advertisement of the Andhra Pharmaceutical Works, Limited, Bezwada.

The Council approved the suggestion made by Dr. V. Rama Kamath that no notice should be taken of any anonymous communication; and directed the Registrar to send a copy of the first part of the resolution passed by the Council in regard to item No. 5 in the agenda to all the registered medical practitioners whose names are associated with the Andhra Pharmaceutical Works, Limited, Bezwada with a suitable covering letter.

Read the Registrar's note requesting the Council to give their opinion on the envelope received by him from the registered medical practitioner, on which the name, qualifications, address, etc., of the practitioner were displayed in a manner likely to be mistaken as an advertisement. The Council was of the opinion that there was no violation of paragraph 6 of the Warning Notice in such cases.

Read letter addressed to the Registrar by Dr. G. Sreemulu, L.C.P. & S. (Bomb.), dated the 2nd March, 1940, complaining that Messrs. Binny & Co., Limited, were forcing passengers to get themselves re-vaccinated by the company's medical officer, in spite of their possessing vaccination certificates issued by the said practitioner, and also the connected papers.

Read also the remarks of the then Vice-President (Dr. T. Satakopan) on the subject.

The Council passed the following resolution:—

"That Messrs. Binny & Co., Ltd., the informed that the monopoly of issuing vaccination certificates by any particular medical practitioner employed under the firm is against the spirit and principles of the Madras Medical Registration Act, and that malpractices relating to the issue of vaccination certificates or any other certificate to the members of the public, if reported to the Medical Council, will be suitably dealt with."

Madras Medical Register—Annual printing and publication of. The following resolution was carried:—"While recording the Government Order (No. 20, P.H., dated 4th January 1940, the Council requests Government to rescind the Government Order, as in the interest of the public and the medical profession the medical register should be published with the least delay as it is the only authentic document in regard to medical registration."

Executive Committee—Appointment of—G.O. Ms. No. 3181, P.H., dated the 2nd Septemer, 1939. The Council, while approving the necessity of a statutory Executive Committee, appointed a special committee consisting of Dr. V. Rama Kamath, Dr. S. Ramakrishnan and Dr. R. J. Dyson (Convener) to go into the subject and submit a report to the Council at their next meeting, regarding the functions, etc., of the Executive Committee, to enable Government to so amend the Act as to provide for an Executive Committee."

Medical Registration—The following resolution was unanimously passed:—"This Council decides to charge a fee of Rs. 5 for registering the names of the medical practitioners borne on the other provincial medical registers, and requests Government to amend section 14 of the Act, making provision for the levy of Rs. 5 for reciprocal registration."

The Council decided unanimously not to enhance the fee for primary registration as suggested in the Government Order No. 4106, P.H., dated the 6th November, 1939.

Madras Medical Registration Act, 1914—Term of office of members elected under section 5 (1) (*c*) to (*e*) of—Alteration of.

The following was passed unanimously:

"The Council agrees to the suggestion made by Dr. V. Rama Kamath (Editor, *Medical Practitioner*) and approved by the Surgeon-General, that the Act should be suitably amended for the termination of the term of office of members elected under section 5 (1) (*c*) to (*e*) soon after they cease to represent the constituencies which elected them."

Change of names of registered medical practitioners—Proposal to levy fee for.

The resolution "That a fee of Rs. 5 for incidental expenses be levied for effecting a change in the name of a registered medical practitioner" was passed *unanimously*.

Names removed from the Medical Register under section 16 (2)—Procedure to be adopted.

The following suggestion was unanimously accepted:

"The Council does not feel the necessity of getting back the certificates of registration from medical practitioners whose names were erased from the Medical Register; and directs the Registrar to notify the erasures of such names in the *Fort St. George Gazette*, in at least two important newspapers, in medical journals and to the Registrars of all Provincial Medical Councils in India."

Medical Registration—Additional qualifications—D.P.H. & Hy. of Calcutta—Recognition of.

Read the letter, dated the 24th July, 1940, from the Honorary Secretary, Faculty of Tropical Medicine and Hygiene, Bengal School of Tropical Medicine, Calcutta.

The Council directed the Registrar to find out and report to the Council at its next meeting, if the Government of Bengal recognized the Faculty of Tropical Medicine and Hygiene, Bengal School of Tropical Medicine, Calcutta.

Medical Registration—Proviso to section 13 of the Madras Medical Registration Act—Application of Dr. Lydia Herlufssen, M.B., CHB. (Copen).

The Council decided that the matter lie over for the present, pending receipt of a reply from Government in regard to the registration of medical missionaries.

Dr. P. A. Rama Ayyar, L.M.P.—Appeal to the Council to reconsider its decision.

After some discussion, the following resolution was passed:—

"This Council resolves to obtain legal opinion through Government regarding the interpretation of sub-section (2) of section 16 of the Madras Medical Registration Act, 1914, as to the powers of the Council to restore the name of a medical practitioner before the expiry of the specific period of suspension."

The following resolutions were passed:

I. "Whereas it is desirable that the elections to the Madras Medical Council be made widely known to the Registered Medical Practitioners, this Council resolves that the elections to the Madras Medical Council be advertised by publishing the notice of election in all the dailies of Madras and by circulating the same to all the Medical Associations in the Province and to the Medical Colleges and City Hospitals for circulation amongst the staff."

II. "Whereas it is desirable that the medical practitioners should have a knowledge of "Medical Ethics", this Council recommends to the Principals of Medical Colleges to arrange for a course of lectures on 'Medical Ethics', professional misconduct and allied subjects to the medical students during their final year of study."

* * * * *

Extracts from proceedings of the General Business Meeting held on 31st March, 1941:

Dr. C. R. Krishnaswami, was declared duly elected Vice-President of the Council.

Dr. R. K. Narasimhachari, L.M.P.—Advertisement by means of handbills—Violation of paragraph 6 of Warning Notice.

Read office note on the subject.

The Council constituted itself as a Court under section 17 (1) of the Madras Medical Registration Act, 1914, and proceeded to deal with the case: (Vide "Proceedings of the Council when constituted as a Court," recorded in the book maintained for the purpose).

Dr. S. Sanjeeva Shenoy, L.M.P., of Tandarampatti—Production of good conduct certificates by.

The following motion was put from the Chair and *carried*:

"The Council having considered Dr. S. Sanjeeva Shenoy's letters, dated the 12th January, 1941, and 24th February, 1941, consider that the excuses advanced by Dr. Sanjeeva Shenoy are unsatisfactory; and

(i) reprove him severely for not obeying the Medical Council's directions in that he submitted the general practitioner's certificate after the 7th January, being the date prescribed and in not having submitted the District Medical Officer's certificate by that date and not even up to the date of the meeting; and

(ii) warn him that if both the certificates of the District Medical Officer and the general practitioner be not received in the President's office before noon on the 7th of April and before noon on the 7th of July and quarterly thereafter, the Council will be compelled to proceed further in the case."

Dr. U. D. Gopal Rao, L.M.P.—Appeal to Government against decision of the Special Committee—Appeal dismissed.

Dr. V. Rama Kamath moved:

"While recording the Government Order (No. Ms. 5468, P.H., dated the 20th November, 1940), the Council feels the necessity of having a provision in the Madras Medical Registration Act, 1914, for appeals by an aggrieved complainant against the decision of the Council in disciplinary cases."

This was seconded by Dr. T. Shenappa Shetty and *passed*.

Medical registration—Recognition of foreign qualifications —Resolution of the Medical Council of India for uniformity of procedure.

Read Government Memorandum No. 2164|40-1 D-1, P.H., dated the 23rd January, 1941 and the office note on the subject.

The following resolution was passed:—

"That with reference to this subject, the Provincial Medical Council will refrain, as far as possible, from recommending for recognition under the Provincial Medical Act, qualifications granted by institutions of other countries."

Medical Registration—Qualifications granted in the Kingdom of Italy, not recognized.

Read and recorded letter from the Registrar, British Medical Council, dated the 17th October, 1940, and the office note on the subject.

Medical Registration—Additional qualification—Recognition of D.P.H. & Hy. (Calcutta).

Read the office note on the subject and also the letter, dated the 11th March, 1941, from the Registrar, Bengal Council of Medical Registration.

The following resolution was passed by the Council:—

"That the Council resolves to postpone decision regarding 'D.P.H. & Hy.' as an additional qualification till the question is decided by the Government of Bengal to whom it has been referred to by the Bengal Medical Council."

Medical Registration—Irregularities in previous years.

Read office note on the subject. Moved from the Chair, and passed, that—"This subject be referred to a Committee consisting of three members (Dr. V. Rama Kamath, Dr. S. Ramakrishna and Dr. C. R. Krishnaswami, Vice-President, as Chairman of the Committee) to investigate the errors and rectify them."

The Registrar was directed to prepare full notes for the information of the Committee.

The following motion was passed:—

"The Madras Medical Council desires to point out to the Government that it is detrimental to the interest of the Medical Profession and the public to fix the maximum age-limit of 35 years for candidates appearing for the T.D.D. diploma, newly instituted by the Madras Government and requests the Government that the maximum age restriction may be done away with."

PERSONNEL OF THE DRUGS TECHNICAL ADVISORY BOARD

The Secretary to the Government of India in a notification No. F.-54-2|40-H. .C) in the Gazette of India, June 14, 1941. announces:

In pursuance of section 5 of the Drugs Act, 1940, XXIII of 1940, the Central Government is pleased to constitute the Drugs Technical Advisory Board consisting of the following members, namely:—

Ex-officio members under clauses (i), (ii), (iii), (iv) and (v) of sub-section (2) of section 5:—

1. The Director-General, Indian Medical Service (Chairman).
2. The Director of the Central Drugs Laboratory.
3. The Director of the Central Research Institute.
4. The Director of the Imperial Veterinary Research Institute, Muktesar.
5. The Chief Chemist, Central Revenues.

Elected under clause (vii) of sub-section (2) of section 5:

6. Dr. B. B. Dikshit, M.B., B.S., D.P.H., M.R.C.P., Ph.D., Haffkine Institute, Bombay (Pharmacologist).
7. Mr. A. F. MacCulloch, M.B.E., M.A., B.SC., F.I.C., A.M.I.CHEM.E., Chief Advisory Chemist, Office of the Director-General, Indian Medical Service (Pharmaceutical Chemist).

Elected under clause (viii) of sub-section (2) of section 5:—

8. Dr. P. Kutumbiah, B.A., M.D. (Mad.), M.R.C.P. (Lond.), Professor of Medicine, Andhra Medical College, Vizagapatam (Teacher of Medicine and Therapeutics).

9. Dr. Badri Narayan Prasad, M.SC., M.B., D.T.M., Ph.D., Professor of Pharmacology, Prince of Wales Medical College, Patna (Teacher of Medicine and Therapeutics).

10. Dr. Jivraj N. Mehta, L.M. & S., M.D., M.R.C.P., F.C.P.S., Dean, Seth Gordhandas Sunderdas Medical College, Bombay (Registered Medical Practitioner).

Nominated under clause (ix) of sub-section (2) of section 5:—

11. Mr. P. Das, PH.D., M.S. in Phar. (Mich.).

Elected under clause (x) of sub-section (2) of section 5:—

12. Professor Bires Chandra Guha, PH.D., D.SC., (Lond.), Ghosh Professor of Applied Chemistry, University College of Science, Calcutta.

13. Professor Mahadev Lal Schroff, A.B. (Cornell), M.S. (Mass.), Professor of Pharmaceutical Chemistry, Hindu University, Benares.

Elected under clause (xi) of sub-section (2) of section 5:—

14. Dr. Anil Kumar Sen, M.B. (Cal.), (elected by the Central Council of the Indian Medical Association).

15. Dr. S. Rajagopal Naidu, B.A., M.B., B.S., M.SC., F.I.C., D.I.C., Chemical Examiner with the Government of Madras and Professor of Chemistry, Madras Medical College, (elected by the branches in India of the British Medical Association).

Secretary appointed under sub-section (7) of section 6:—

Mr. A. F. MacCulloch, M.B.E., M.A., B.SC., F.I.C., A.M.I.CHEM.E.

DR. H. DE SA SILVER JUBILEE PRIZE

The Bombay Obstetric & Gynæcological Society has selected Metabolism in Pregnancy as the subject for the thesis for the above prize for 1941-42. The prize is open to all medical practitioners registered with the Bombay Medical Council. The last date for receiving the thesis is 15th March, 1942.

BOMBAY MEDICAL COUNCIL

The following summary of the proceedings of the Meeting of the Bombay Medical Council held on the 10th February, 1941 is published for general information:—

The Council elected the following six members to the Executive Committee for the year 1941-42:—Lieut.-Col. S. L. Bhatia, M.C., M.A., M.D., I.M.S., J.P. Drs. B. G. Vad, M.D., F.C.P.S., C. A. Amesur, M.S., M.R.C.S., L.R.C.P.S., D.L.O., George Coelho, M.B.B.S., M.R.C.P., B.Hy., U. B. Narayanrao, L.C.P.S., and V. D. Sathaye, B.Sc., L.C.P.S.

With regard to the adjourned consideration of complaint against Dr. J. J. Cursetji, M.D., L.R.C.P. & S., etc., in respect of the publication of an article in the *Insurance World* of February 1939 and several statements made therein, it was decided that Dr. Cursetji's letter of explanation and regret be accepted and the papers recorded.

It was decided that the consideration of the complaint against Dr. J. P. Chobhe, M.B.B.S., Nasik, for infringement of the provisions of clause 1(*b*) of Section II of the Code of Medical Ethics as per the resolution of the Executive Committee in that behalf, be adjourned to the next session of the Council.

With reference to the Report of the Sub-Committee in respect of the Notice of Motion by Dr. Jivraj Mehta regarding amendment in section 3 of the Schedule to the Bombay Medical Act, 1912, and the memorandum from the Surgeon General with the Government of Bombay and its accompaniments, on the question of recognition of medical degrees by Provincial Medical Councils, of Licensing Bodies outside British India, pending amendment of the Indian Medical Council Act, 1933, investing the Medical Council of India with powers to have an All India Register, it was decided that the object the Medical Council of India had in view could best be achieved by Central Legislation on the subject, and pending the same, by the Provincial Medical Councils recognising for registration qualifications laid down in Schedule II of the Medical Council of India Act, 1933, only. It was also decided to recommend to Government that pending the proposed legislation by the Government of India regarding amendment of Indian Medical Council Act, 1933, on the question of recognition of Licensing Bodies outside India, qualifications of all non-Indian Licensing Bodies not on the Second Schedule to the Medical Council of India Act, 1933, be deleted from the Schedule to the Bombay Medical Act, 1912.

The recommendations of the Sub-Committee in respect of the Notice of Motion proposed by Dr. Gadgil and seconded by Dr. Coelho regarding amendments in the Rules of the Council relating to election were accepted subject to certain amendment being incorporated therein.

The Committee's recommendation in respect of a resolution adopted by the Council relating to the amendment of the Bombay Medical Act, VI of 1912, was accepted.

It was decided that having regard to the practice obtaining in other Provinces, the courtesy title of "Dr." should be prefixed hereafter in the case of all medical practitioners registered under the Bombay Medical Act, 1912.

The motion of Dr. U. B. Narayanrao expressing the Council's opinion that in order to have a uniform Code of Medical Ethics for the whole of India, the Medical Council of India be requested to convene a representative Conference of all the Provincial Medical Councils or Boards constituted under an Act of Provincial Legislature, was lost.

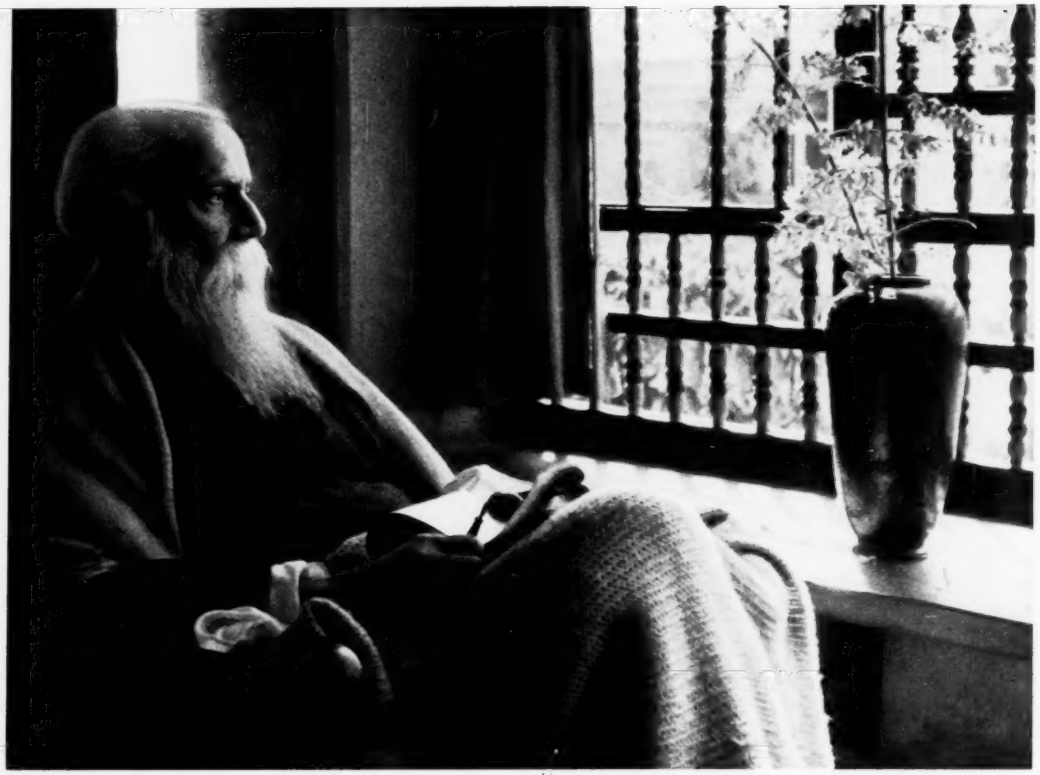
With refernce to the memorandum from the Surgeon General with the Government of Bombay requesting the views of the Council on the proposed amendment to the Government Resolution, General Department, No. 7898, dated 6th November 1939, relating to the registration of persons holding qualifications from the College of Physicians and Surgeons, Calcutta, in 1909, it was decided that no amendment in the orders contained in the Government Resolution was necessary and that such cases of those practitioners only who are domiciled in the Province of Bombay or Sind should be considered hereafter.

It was decided that in the opinion of the Council for paragraph 1 (1) of Government Resolution, General Department, No. 7898, dated 6th November 1939, regarding recognition of qualifications of certain Calcutta institutions obtained between the years 1912 to 1916 (both inclusive), the following be substituted:—

"The National Medical College and the National College of Physicians and Surgeons, Calcutta."

With reference to the letter from the Surgeon General with the Government of Bombay requesting the viws of the Council on the question of proposed legislation to amend the Indian Medical Council Act, 1933, in order to empower the Council to appoint "Visitors" in addition to Inspectors, it was decided that the proposed legislation respecting the appointment of visitors by the Medical Council of India, was not necessary.

The resolution given notice of by Dr. Mrs. K. Tarabai, seconded by Dr. Amesur, regarding proposed amendment of some provisions of clause 1 of Section II of the Code of Medical Ethics relating to certain Objectionable Practices, was referred to the Executive Committee for report.



The Last Portrait of the Poet

By courtesy
The Calcutta Municipal Gazette

By : *Jitendra Pratap Singh*
Santiniketan

Engraved & printed by
The Bengal Autotype Co., Cal.

RABINDRANATH

RABINDRANATH is no more!

With him closes an age, which will be ever associated with his great name. It is not possible for us, his contemporaries, to give adequate expression to our sense of profound loss.

RABINDRANATH, with his songs and poems, with his infinite variety of expression and his manifold activities, belonged essentially to the young. They have grown up in the tradition of his greatness, and for them the death of their beloved *Kavi-guru* has created a void which it will be impossible to fill.

THE name of Rabindranath remains enshrined in our hearts. Upon his shoulders fell the mantle, which came down through the ages from Valmiki to Kalidas and now too he has joined the immortals.

MAY his soul rest in peace.

M. Natarajan

THE POET'S LAST PRAYER

O Pilot of my life,
cast loose the moorings
of this frail vessel,
for before me
lies the vast ocean of Peace.

Comrade of mine for ever,
take me and hold me close.
The lode-star will shed
its steadfast glow
on the never-ending path to Eternity.

O Saviour,
Your mercy and forgiveness
are the inexhaustible wealth
on which I draw
for this my last journey.

May the bonds of mortality melt away,
may the vast universe take me in its arms,
and may it be given me
fearlessly to stand face to face
before the Great Unknown.

All rights reserved by Visva-Bharati.

JOURNAL
OF THE
INDIAN MEDICAL ASSOCIATION
Vol. X. No. 11. August, 1941